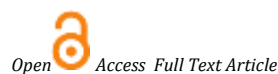


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Case Report

High concentration Amiodarone continuous infusion induced Phlebitis: A Case Report

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Abstract

Phlebitis caused by high concentration amiodarone infusion is a rather uncommon occurrence. Phlebitis is one of the most reported causes of high concentration amiodarone continuous infusion in bradycardia. We reported a case of patient with continuous infusion of amiodarone induced phlebitis. Patient felt pain along the path of cannula, erythema, induration, palpable venous cord. Visual Infusion Phlebitis Score was assessed and VIP Score was found to be 4. We suspected the incidence of phlebitis due to high concentration and continuous infusion of IV amiodarone. In this case report, we would like to discuss about the standard protocol of IV administration of amiodarone, evaluation of phlebitis by Visual Infusion Phlebitis Score, and management of Phlebitis.

Keywords: Visual Infusion Phlebitis Score, amiodarone, phlebitis, tachyarrhythmia, peripheral administration.

Introduction:

The American Heart Association's Advanced Cardiac Life Support algorithms for ventricular tachycardia/ventricular fibrillation list intravenous amiodarone as the first-line therapy as the gold standard for treating patients with rhythm-related tachyarrhythmias. This includes atrial fibrillation, atrial flutter, and ventricular tachycardia^{1,2}. Amiodarone is an anti-arrhythmic agent; it was first introduced in 1961 as a drug for treating angina which work by relaxing overactive heart muscles³. Amiodarone has a solution osmolality between 255 to 345 mOsm/L and a pH between 3.46 to 4.35, which increases the risk of damaging vein intima and may result in chemical phlebitis with an incidence between 5%-85%, depending on the specific infusion protocol⁴⁻⁹.

In accordance with definitions, phlebitis is an inflammation of the tunica intima of the vein that can produce discomfort, tenderness, oedema, and erythema. The skin is also hot to the touch and may have a palpable cord¹⁰⁻¹². Numerous factors, including concentrations above 2 mg/mL, a higher amiodarone dose, peripheral lines, speed of administration,

duration of amiodarone administration, lack of in-line filters, suboptimal aseptic technique during line insertion, lack of post-infusion line flushing, poor vein condition, older age, female sex, administration errors, drug stability, amiodarone pH, host factors, and concussion, are linked to blood vessel irritation¹²⁻¹³. Phlebitis can be physical, chemical, or infective. Physical causes of phlebitis include catheter material, length, & lumen size, and poor insertion technique and/or maintenance and chemical causes include concentration, solution dilution, speed of administration, & precipitate formation, osmolality [255-345 mOsm/L] & pH [3.46-4.35]. During amiodarone infusion, needle-shaped crystals can form and damage local tissue. This crystallization may occur at any time during administration. Amiodarone may disintegrate into particles while being stored as a result of the medication's instability, low quality assurance, or inferior compounding processes. Furthermore, plasticizers from polyvinyl chloride that are likewise irritating to the vessel wall can be leached away by amiodarone. Higher amiodarone concentrations and lower flow rates result in more leaching¹⁴. Large catheters inserted into small veins result in trauma, a drug with pH less than 7 & specially those with less than 4.1 can harm the vein

intima or intima of the vein & placing small catheter in a large vein had less chances of phlebitis. The greatest technique to lower incidence of phlebitis is via hemodiluting acidic infusions. Due to better blood flow, the Infusion Nurses Society also suggests administering in a big vein¹¹.

Case Report:

A 60-year-old male patient with K/C/O of Ca Esophagus who underwent Feeding Jejunostomy on 15/12/2022 admitted for supportive care with the chief complaints of loss of appetite, abdominal pain and fever for 3 days with abnormal vitals such as BP: -73/44mmHg, PR: - 111bpm, SpO₂: - 70%, Temp: - 96.7°F. The patient is well managed with 1 Unit of DNS bolus, DNS/RL @75ml/hr, O₂ 2L, and other supportive therapy.

On day 2, at 9pm patient went on Bradycardia and Hypotension with PR: - 25bpm, BP: -70/50mmHg, SpO₂: - 94% on 3 liters of O₂. The patient was shifted from general ward to ICU and Intensivist advised Inj. Norad 2amp+46ml NS @ 10ml/hr and Inj. Amiodarone 600mg+50ml NS @ 5ml/hr @ 9:30pm and 9:50pm respectively. Inj. Amiodarone stopped on 11pm as patient was stable with vitals BP: - 100/60mmHg, PR: - 76bpm, SpO₂: - 96% with O₂ and Inj. Norad was on flow @10ml/hr.

On day 3, suspecting bilateral lower lobes pneumonia (viral?) consultant advised Tab. Levoflox 500mg 0-1-0, Cap. Fluvir 75mg 1-0-1 for 5 days.

On day 4, at 11am Inj. Norad was stopped as patient was stable with vitals PR: -90bpm, BP: -120/80mmHg, SpO₂: -

91%. At 5pm patient suddenly developed AF and went on Hypotension with vitals PR: - 170bpm, BP: - 104/66mmHg, RR: - 22cpm, Intensivist advised 300mg Inj. Amiodarone bolus followed by 2.5-5 ml/hr infusion for 18 hours along with Inj. Clexane 40mg BD. The first bolus Inj. Amiodarone 150mg is given at 5pm and second bolus 150mg at 5:30pm followed by Inj. Amiodarone infusion started at 4ml/hr with concentration of 12mg/ml and Inj. Norad at 2ml/hr, by 9pm on the same day Inj. Amiodarone was stopped as vitals were BP: - 120/78mmHg, PR: - 68bpm, Temp: - 97.6 F, SpO₂: - 94% on O₂.

On day 5, at 10:30am Inj. Noradrenaline tapered to 0.5ml/hr and stopped, the morning shift staff has observed the pigmentation on the left arm around the cannula site which was purplish in appearance, severe pain on touch and induration (as shown in Figure). Consultant advised stat Inj. Clexane 40mg S/c BD and Inj. Amiodarone was switched from Inj. to Tab BD, consultant suggested to apply Thrombophob ointment to the pigmented skin twice a day. The pigmentation is dressed with MgSO₄ (magsulf dressing) and neatly covered with gauze.

On day 7, the dressing was removed, the blisters occurred on the pigmented area with reduced pain on touch and induration. The patient is discharged on day 12th with medications Tab. Levoflox 500mg 1-0-1 BD for 2 days, Tab. Pantop 40mg 1-0-0 for 5 days, Tab. Forcan 150mg 1-0-0 for 2 days, Tab. Bactrim DS 2-2-2 for 2 days, Tab. Dolo 650 1-1-1 for 5 days, Tab. Cardrone 100mg 1-0-1 to continue and Tab. Montac-LC 0-0-1 for 10 days, Syp. Grilinctus BM 10ml TID, Tab. Equilis 5mg 1-0-1 to continue.

Table 1: Vitals of the patient during hospitalization

Date	BP (mmHg)	PR (bpm)	RR (cpm)	SpO ₂ (%)	Temp. (F°)
14/2/23	90/60	110	20	93.0	100.6
15/2/23	95/60	68	18	95.0	97.0
16/2/23	110/70	82	18	98.0	98.6
17/2/23	110/70	82	18	97.0	98.6
18/2/23	120/70	71	22	96.0	97.4
19/2/23	132/78	72	16	90.0	98.4
20/2/23	130/82	72	16	94.0	98.6
21/2/23	130/80	90	18	97.5	97.0
22/2/23	120/80	88	18	98.0	97.0
23/3/23	130/80	92	20	97.0	97.0



Figure 1: - Day 5



Figure 2: - Day 8



Figure 3: - Day 9



Figure 4: - Day 10



Figure 5: - Day 11



Figure 6: - Day 12

Visual Infusion Phlebitis Score IV site appears healthy	0 No signs of phlebitis OBSERVE CANNULA
One of the following is evident: • Slight pain at IV site • Redness near IV site	1 Possible first sign of phlebitis OBSERVE CANNULA
Two of the following are evident: • Pain • Erythema • Swelling	2 Early stage of phlebitis RESITE THE CANNULA
All of the following signs are evident: • Pain along the path of the cannula • Erythema • Induration	3 Medium stage of phlebitis RESITE THE CANNULA CONSIDER TREATMENT
All of the following signs evident and extensive: • Pain along the path of the cannula • Erythema • Induration • Palpable venous cord	4 Advanced stage of phlebitis or start of thrombophlebitis RESITE THE CANNULA CONSIDER TREATMENT
All of the following signs are evident and extensive: • Pain along the path of the cannula • Erythema • Induration • Palpable venous cord • Pyrexia	5 Advanced stage of thrombophlebitis INITIATE TREATMENT RESITE THE CANNULA

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Figure 7: - By assessing the patient's symptoms we found the **VIP Score 4**.

Discussion:

The concentration of amiodarone, an iodinated benzofurane derivative, the amount of amiodarone in given volume which is measured in mg/ml. Rate of administration is the desired rate at which a drug should be administered to achieve a steady state of a fixed dose which has been demonstrated to be therapeutically effective.

Protocol for IV administration of Amiodarone: -

Use an in-line filter when administering amiodarone with a volumetric infusion pump, preferably through a central venous catheter. For peripheral vein infusions lasting more than an hour, concentrations should ideally not be higher than 2 mg/mL; central line administration at doses higher than 2

mg/mL is preferred¹⁵. Glass or polyolefin bottles containing D5W must be used to provide infusions lasting more than two hours. Amiodarone in PVC container is stable for up to 2 hours at room temperature diluted with D5W to concentration of 1-6 mg/ml & the same diluted solution is stable for up to 24hours in polyolefin or glass container.

Quick loading IV infusion of 150mg given over 10 minutes i.e., 15mg/min, at a concentration of 1.5mg/ml which is prepared by diluting 50mg/ml of 3ml vial in 100ml D5W followed by slow loading IV infusion of 360mg over 6 hours at 1.8mg/ml concentration. After that, provide a 540 mg maintenance infusion over 18 hours (0.5 mg/min). After the initial 24 hours, a maintenance infusion at a rate of 0.5 mg/min and a concentration of 1 to 6 mg/mL should be continued. For

breakthrough arrhythmias, administer additional doses of 150 mg IV over 10 minutes (15 mg/min) mixed in 100 mL of D5W. Initial infusion rates shouldn't be higher than 30 mg/min, however maintenance infusion rates can be raised for more successful arrhythmia suppression¹⁶.

In our case, Clinical Pharmacologist intervened that the infused drug amiodarone was diluted with NS to the concentration of 12mg/ml (which is exceeding standard protocol which is 2mg/ml) and infused by DEHP free PM-O-LINE which doesn't contain any in-line filter. The infusion pump was used to administer Amiodarone through peripheral vein by 18G catheter with 4ml/hr infusion rate. The CP also intervened that the reconstituted amiodarone was infused to the patient over 6 hours after 24 hours of reconstitution. The Inj. Amiodarone was infused to patient at 48mg/hr over 4 hours. All these parameters might have led the patient to Phlebitis.

Conclusion:

Amiodarone should be infused according to the standard protocol, if not the patient can develop pain, tenderness, oedema, and erythema that leads to phlebitis which in turn increases the hospital stay and additional cost burden to the patient and also serious complications were associated with phlebitis.

Peripheral administration of amiodarone should be avoided and administration of central vein should be preferred if amiodarone is administered peripherally, then the Protocol of IV amiodarone administration should be followed sincerely. Nursing staff should monitor further administration of IV amiodarone in similar patients which can reduce the incidence of phlebitis, and they must monitor the concentration, rate, diluent used for, and IV site of amiodarone administration. Once the drug is administered the nursing staff should keep on observing the patient's IV site for pain, tenderness, oedema, and erythema if there are any such symptoms the drug should be discontinued immediately and managed appropriately.

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Conflict of Interest

The authors declare no conflict of interest.

Abbreviations:

mOsm/L: The number of milliosmoles of the solutes per liter of solution; **AF:** Atrial fibrillation; **RR:** Respiratory rate; **K/C/O:** Known case of; **Ca:** Carcinoma; **BP:** Blood pressure; **PR:** Pulse rate; **SpO₂:** Oxygen saturation; **Temp:** Temperature;

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