Assessment of phlebitis and infiltrations following standard versus high concentration amiodarone boluses in hospitalized adult patients without central venous access

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Disclosure Statement

- IRB Status: Approved
- Co-investigators:
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- Conflicts of Interest: None
- Project Sponsorship: None

IRB: Institutional Review Board

Learning Objectives

- Describe the association of phlebitis and infiltrations with peripheral amiodarone intravenous administration and current practices to decrease the risks
- Compare the incidence of phlebitis and infiltrations in standard versus high concentration amiodarone boluses

Background

- Administration of intravenous (IV) amiodarone is associated with phlebitis and infiltrations
  - Reported incidence 13.9% - 85%
- Proposed mechanism is related to formation of precipitants in the vein surrounding the infusion site

- Mowry JL, et al. *West J Nurs Res.* 2011;33(3):457-71.
- Spiering M. *J Infus Nurs.* 2014;37(6):453-60.
- Slim AM, et al. *Mil Med.* 2007;172(12):1279-83.
- Boyce BA, et al. *Crit Care Nurse.* 2012;32(4):27-34.

Background

- Factors related to development of phlebitis and infiltrations
  - Low pH
  - High concentration (>3 mg/mL)
  - Administration via a peripheral venous catheter (PVC)
  - Longer duration of therapy
  - Higher medication dose

- Spiering M. *J Infus Nurs.* 2014;37(6):453-60.
- Nexterone [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2011.
- Norton L, et al. *Am J Crit Care.* 2013;22(6):498-505.

Background

- Manufacturer recommendations to prevent phlebitis and infiltrations with amiodarone administration:
  - Central venous catheter (CVC) with in-line filter
  - If PVC used:
    - Maximum recommended concentration is 2 mg/mL

PVC: peripheral venous catheter; mg: milligrams; mL: milliliters

- Nexterone [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2011.

Background

- 2017 nationwide IV fluid shortage impacted the supply of dextrose available to compound amiodarone bolus doses
- At Billings Clinic:
  - Unstable patients received standard amiodarone bolus (concentration 1.45 mg/mL)
    - Available on floor
  - Clinically stable patients received amiodarone bolus from large volume continuous infusion product (concentration 1.74 mg/mL)
    - Compounded in main pharmacy

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Purpose

- Determine the effect of different concentrations of amiodarone boluses on the incidence of phlebitis and infiltrations in hospitalized adult subjects with PVCs who are receiving IV amiodarone

PVC: peripheral venous catheter

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Methods: Study Design

- Single-center
- Prospective
- Observational

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Methods: Inclusion Criteria

- Age ≥18 years
- Admitted to Billings Clinic hospital between August 2017 and March 2018
- Administered ≥1 IV amiodarone bolus dose ± infusion via a PVC

PVC: peripheral venous catheter

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Methods: Exclusion Criteria

- Pregnant or breastfeeding
- Presence of a CVC

CVC: central venous catheter

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Methods: Study Groups

- Bolus dose: 150 mg IV over 10 minutes
  - Standard concentration (SC): 1.45 mg/mL
    - 150 mg/3 mL in 100 mL D5W
    - Total bolus volume: 103 mL (separate IV piggyback)
  - High concentration (HC): 1.74 mg/mL
    - 900 mg/18 mL in 500 mL D5W
    - Total bolus volume: 86 mL (from IV infusion bag)

D5W: dextrose 5% in water

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Methods: Primary Outcome

- Incidence of phlebitis or infiltration in patients receiving IV amiodarone boluses via PVCs

PVC: peripheral venous catheter

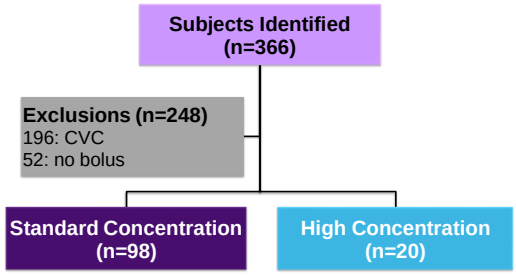
Methods: Secondary Outcomes

- Grade of phlebitis or infiltration
- Time to onset of phlebitis or infiltration (hours)
- Total duration of amiodarone IV bolus ± infusion (hours)
- Total IV amiodarone dose (mg)

Methods: Statistics

- Sample size
  - On average, 40 amiodarone bolus doses ordered per month
  - Convenience sample of 352 subjects
- Statistical tests
  - Descriptive statistics
  - T-test
  - Chi-square test

Results: Study Subjects



CVC: central venous catheter

Results: Baseline Characteristics

Characteristic	All Subjects (n=118)	SC (n=98)	HC (n=20)
Age (years), mean ± SD	71.4 ± 11.6	71.5 ± 11.2	70.6 ± 13.9
Female, n (%)	41 (34.7%)	37 (37.8%)	4 (20%)
Length of stay (days), mean ± SD	7.6 ± 8.9	8.1 ± 9.6	5.1 ± 3

HC: high concentration; SC: standard concentration

Results: Baseline Characteristics

Indication, n (%)	All Subjects (n=118)	SC (n=98)	HC (n=20)
Atrial fibrillation/flutter	91 (77.1%)	73 (74.5%)	18 (90%)
Ventricular tachycardia	20 (16.9%)	18 (18.4%)	2 (10%)
Supraventricular tachycardia	1 (0.8%)	1 (1%)	0
Ventricular fibrillation	4 (3.4%)	4 (4%)	0
Premature ventricular contraction	2 (1.7%)	2 (2%)	0

HC: high concentration; SC: standard concentration

Results: Incidence of Phlebitis and Infiltrations

Characteristic, n (%)	All Subjects (n=118)	SC (n=98)	HC (n=20)	P Value
Phlebitis	37 (31.4%)	29 (29.6%)	8 (40%)	0.36
Infiltration	33 (28%)	27 (27.6%)	6 (30%)	0.82
Phlebitis and Infiltration	29 (24.5%)	23 (23.5%)	6 (30%)	-

HC: high concentration; SC: standard concentration

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Results: Grade of Phlebitis and Infiltrations

Characteristic, n (%)	All Subjects	SC	HC	P Value
PHLEBITIS	n=37	n=29	n=8	
Low Grade (1 – 3)	28 (75.7%)	24 (82.8%)	4 (50%)	0.056
High Grade (4 – 5)	9 (24.3%)	5 (17.2%)	4 (50%)	
INFILTRATION	n=33	n=27	n=6	
Low Grade (1 – 2)	28 (84.8%)	23 (85.2%)	5 (83.3%)	0.91
High Grade (3 – 4)	5 (15.2%)	4 (14.8%)	1 (16.7%)	

HC: high concentration; SC: standard concentration

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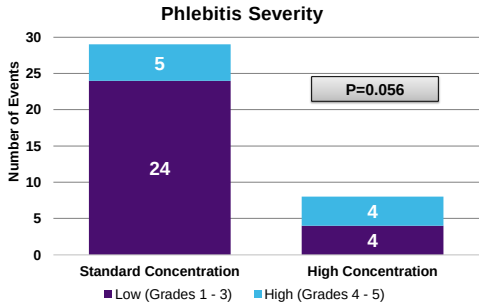
Results: Grade of Phlebitis



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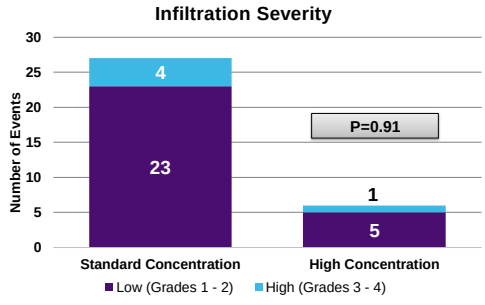
Results: Grade of Infiltrations



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Results: Time to Onset of Phlebitis and Infiltration

Characteristic, mean ± SD	All Subjects	SC	HC	P Value
PHLEBITIS	n=37	n=29	n=8	
Time to Onset (hours)	23.8 ± 16.7	22.8 ± 14.8	27.5 ± 23.4	0.49
INFILTRATION	n=33	n=27	n=6	
Time to Onset (hours)	25.5 ± 15.8	25.7 ± 13.7	24.4 ± 24.9	0.86

HC: high concentration; SC: standard concentration

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Results: Total Amiodarone Duration and Dose

Characteristic, mean ± SD	All Subjects (n=118)	SC (n=98)	HC (n=20)	P Value
Duration of Therapy (hours)	29.9 ± 30.6	31.3 ± 32.2	22.9 ± 20.7	0.27
Total Dose (mg)	1225 ± 941	1244 ± 982	1132 ± 720	0.63

HC: high concentration; SC: standard concentration

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Results: Infiltration Predictive Model

Variable	P Value
Concentration of bolus	0.21
Age	0.70
Sex	0.44
Total dose	0.49
Concurrent medications through same IV line	0.49
Phlebitis	<0.0001

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Discussion

- No significant difference in the incidence of phlebitis or infiltrations
  - Phlebitis: standard (29.6%) vs. high (40%)
  - Infiltrations: standard (27.6%) vs. high (30%)
- Prior study comparing low (1.2 mg/mL) vs. standard (1.8 mg/mL) amiodarone infusion concentration
  - Phlebitis: low (5.8%) vs. standard (15.6%)

• Mowry JL, et al. *West J Nurs Res.* 2011;33(3):457-71.

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Discussion

- In patients who developed phlebitis, there was a greater incidence of low grade severity in the standard concentration group vs. high concentration group (50% vs. 82.8%, p=0.056)
- No difference in severity of infiltrations between groups
- Mean time to onset of the adverse event was comparable between groups
  - Phlebitis: standard (22.8 hours) vs. high (27.5 hours)
  - Infiltrations: standard (25.7 hours) vs. high (24.4 hours)

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Discussion

- Similar mean duration of amiodarone therapy
  - Standard: 31.3 hours vs. high: 22.9 hours
- Similar average total amiodarone dose
  - Standard: 1244 mg vs. high: 1132 mg

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Limitations

- Small sample size in high concentration group
- Many factors can affect phlebitis and infiltrations
  - Other irritant or vesicant medications
  - Size of IV line
  - Duration of therapy

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Conclusions

- Standard and high concentration amiodarone boluses had similar rates of phlebitis and infiltrations
  - If phlebitis occurred in high concentration group, it was more likely to be a severe grade than in the standard concentration group
  - Phlebitis may be a predictor of future infiltration

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Future Directions

- Anticipate returning to standard concentration amiodarone bolus products
- Share study results with key stakeholders
  - IV Nursing Resource Group
  - Cardiology nurses and providers

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Acknowledgements

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Questions?

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Supplementary Slides

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Clinically Unstable Criteria

- SBP <90 mmHg
- HR >140
- Chest pain, diaphoresis, or shortness of breath
- Presence of arrhythmia

SBP: systolic blood pressure; HR: heart rate

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Phlebitis Scale

Grade	Clinical Criteria
0	IV site appears healthy
1	Slight pain or redness near IV site
2	Two of the following present: • Pain • Erythema • Swelling
3	Both of the following present: • Pain • Induration
4	All of the following present: • Pain • Induration • Erythema • Palpable venous cord
5	All of the following present: • Pain • Induration • Erythema • Palpable venous cord • Pyrexia

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Infiltration Scale

Grade	Clinical Criteria
0	No symptoms
1	• Skin blanched • Edema <1 inch
2	• Skin blanched • Edema 1 – 6 inches
3	• Skin blanched or translucent • Gross edema >6 inches • Mild-moderate pain • Possible numbness
4	• Skin blanched, translucent, discolored • Gross edema >6 inches • Moderate-severe pain • Capillary refill >3 seconds • 3+ pitting tissue edema

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Results: Phlebitis Predictive Model

Variable	P Value
Concentration of bolus	0.24
Age	0.92
Sex	0.33
Total dose	0.9
Concurrent medications through same IV line	0.23
Infiltration	**<0.0001**

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Results: Baseline Characteristics

IV Location, n (%)	All Subjects (n=118)	SC (n=98)	HC (n=20)
Antecubital	53 (44.9%)	46 (46.9%)	7 (35%)
Forearm	46 (39%)	35 (35.7%)	11 (55%)
Hand	7 (5.9%)	7 (7.1%)	0
Upper arm	8 (6.8%)	6 (6.1%)	2 (10%)
Wrist	4 (3.4%)	4 (4.1%)	0

HC: high concentration; SC: standard concentration

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Results: Baseline Characteristics

IV Gauge, n (%)	All Subjects (n=118)	SC (n=98)	HC (n=20)
16	1 (0.8%)	1 (1%)	0
18	34 (28.8%)	27 (27.6%)	7 (35%)
20	65 (55.1%)	56 (57.1%)	9 (35%)
22	15 (12.7%)	11 (11.2%)	4 (20%)
Unknown	3 (2.5%)	3 (3.1%)	0

HC: high concentration; SC: standard concentration

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Results: Concurrent Medications

Characteristic, n (%)	All Subjects (n=118)	SC (n=98)	HC (n=20)
Concurrent Medication	4 (3.4%)	4 (4.1%)	0
Concurrent Vesicant or Irritant	0	0	0

HC: high concentration; SC: standard concentration

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Results: Phlebitis Treatment

Characteristic, n (%)	All Subjects (n=118)	SC (n=98)	HC (n=20)
Cold Compress	3 (2.5%)	2 (6.9%)	1 (12.5%)
Ice	13 (11%)	10 (34.5%)	3 (37.5%)
Observe	20 (16.9%)	16 (55.2%)	4 (50%)
Warm Compress	1 (0.8%)	1 (3.4%)	0

HC: high concentration; SC: standard concentration

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Results: Infiltration Treatment

Characteristic, n (%)	All Subjects (n=118)	SC (n=98)	HC (n=20)
Cold Compress	5 (4.2%)	4 (14.8%)	1 (16.7%)
Ice	14 (11.9%)	11 (40.7%)	3 (50%)
Observe	13 (11%)	11 (40.7%)	2 (33.3%)
Warm Compress	1 (0.8%)	1 (3.7%)	0

HC: high concentration; SC: standard concentration

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