Incidence and Severity of Phlebitis in Patients Receiving Peripherally Infused Amiodarone

Brenda A. Brady Boyce, RN, EdD  
Barbara Horner Yee, RN, MSN, CCRC

**BACKGROUND**  Nurses noted that the rate of phlebitis was high when intravenous amiodarone was infused via a peripheral site. Hospital policy recommends a central vascular catheter, but this method is often not feasible because the drug is administered in emergent situations for short periods.

**OBJECTIVE**  To determine the rate and severity of phlebitis in patients given peripherally infused amiodarone.

**METHODS**  The literature, policy, and procedures for administration of amiodarone were reviewed; the pharmacy was consulted; and a data collection tool was developed. The tool was pilot tested and revised, and face validation was established. Data were collected during a 6-month period. A convenience sample was used.

**RESULTS**  The study included a total of 12 patients. Each new infusion of intravenous amiodarone was considered a separate occurrence, for a total of 24 infusions. Various grades of phlebitis developed in 8 patients (67%). Phlebitis developed at 12 of the 24 infusion sites (50%).

**CONCLUSIONS**  Patients receiving peripherally infused amiodarone are at high risk for phlebitis. This complication may lead to infection, additional medical intervention, delay in treatment, and prolonged hospitalization. (Critical Care Nurse. 2012;32[4]:27-34,71)

Intravenous amiodarone is a class III antiarrhythmic agent commonly used in emergent situations for patients who have unstable atrial and ventricular tachyarrhythmias. Nurses in the progressive care unit at Mount Auburn Hospital, Cambridge, Massachusetts, a community teaching hospital, noticed a high rate of phlebitis when intravenous amiodarone was administered via a peripheral catheter with an in-line filter. Although the preferred method of administration is via a central catheter with an in-line filter, this method is not always feasible because the drug is often administered in emergent situations for a short period. Further, introduction of a central catheter exposes patients to risks and complications such as thrombotic events and mechanical complications (arterial puncture, hematoma, pneumothorax), which have occurred at a rate of 15%.

The hospital's protocol for administration of intravenous amiodarone is consistent with manufacturers' recommendations. Amiodarone is delivered from the pharmacy in a glass intravenous bottle and is administered by using an in-line filter. The filter is required because amiodarone quickly precipitates when mixed with intravenous fluid, a characteristic that can be a factor in the development of phlebitis.

With programmable infusion pumps, the initial bolus dose of 1.5 mg/mL delivered at a rate of 15 mg/min is infused for 10 minutes (total dose, 150 mg). This infusion is followed by a step-bolus dose of 1.8 mg/mL delivered at a rate of 1 mg/min for 6 hours (total dose, 360 mg) and a maintenance dose of 0.5 mg/min for 18 hours (total dose, 540 mg). Although the amiodarone was infused at the recommended rate
and concentration, nurses reported frequent episodes of phlebitis (tenderness, redness, and swelling) during the early administration of amiodarone via a peripheral infusion site.

**Purpose of the Project**

The purpose of this project was to determine the incidence and severity of phlebitis in patients who received intravenous amiodarone via a peripheral catheter in order to evaluate the magnitude of the problem at Mount Auburn Hospital. Phlebitis adversely affects patient care; it may interfere with the continued infusion of amiodarone, necessitate insertion of another peripheral intravenous or central catheter, and extend hospitalization. Further, patients who have phlebitis experience pain, swelling, and inflammation.

**Literature Review**

A literature review was conducted by using CINAHL, MEDLINE, and Cochrane Central Register of Controlled Trials from the earliest searchable databases through September 2010. Search terms were amiodarone, peripheral intravenous, intravenous, phlebitis, thrombophlebitis, and adverse events.

A total of 9 articles addressed the issue of phlebitis and intravenous amiodarone (Table 1). Although the literature consistently reveals that patients receiving intravenous amiodarone are at risk for phlebitis, a different sample population, dosage, route of administration, and method of data collection were used in each study, making it difficult to ascertain the true rate of phlebitis associated with use of the drug. Manufacturers reported that phlebitis occurred at doses greater than 3 mg/mL but stated that the complication could be minimized by using a more dilute concentration of 2.5 mg/mL and in-line filters. Early studies indicated the risk for phlebitis with higher doses of intravenous amiodarone than the dose currently recommended and suggested that amiodarone be infused via a central catheter or changed to oral administration if a patient’s clinical condition is stable. In more recent studies, researchers compared the rate of phlebitis with dosages at or less than the manufacturers’ recommendation. However, in each study, phlebitis was considered a continued problem and concern.

**Methods**

The institutional review board of the hospital was consulted, and the project was considered exempt from review. Before the project was started, the hospital’s nursing policies and practices were evaluated to ensure consistency of administration of intravenous amiodarone. The project team assigned for the study included 1 intravenous therapy nurse, 3 critical care nurses, 1 cardiovascular nurse specialist, and 1 research advisor. A descriptive design was used.

**Draft Data Collection Tool**

A draft data collection tool was developed by the project team after a discussion to determine variables that would affect the development of phlebitis. The tool included each patient’s name, medical record number, date and site of insertion of an intravenous catheter, time for each notation, gauge of intravenous needle, grade of phlebitis if present, and a comment section. A phlebitis rating scale ranging from 0 (no clinical signs or symptoms) to 4+ (severe signs and symptoms including a palpable venous cord) to describe the presence and severity of phlebitis (Table 2) was included on the tool to help ensure interrater reliability. The scale was adapted from the Infusion Nursing Standards of Practice on the recommendation of the intravenous therapy team. For the purposes of this project, and on the advice of the experts on the intravenous team who served as members of the project team, any patient’s report of pain was considered indicative of phlebitis at the intravenous site. The draft tool was presented to members of the nursing research council to establish face validity. Members of the council served as a panel of experts; the council consisted of 18 practicing nurses: 3 intravenous therapy nurses, 4 critical care nurses, 1 cardiovascular nurse specialist, 1 nurse administrator, 1 skin care

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**Authors**

Brenda A. Brady Boyce is executive manager of assessment and remediation for Readypoint Nursing at Pearson Education in Boston, Massachusetts. Barbara Homer Yee is a project and database manager, Department of Cardiology, Mount Auburn Hospital, Cambridge, Massachusetts, and a member of the nursing research council. Corresponding author: Brenda A. Brady Boyce, RN, EdD, Executive Manager, Assessment and Remediation, Readypoint Nursing, Pearson Education, 75 Arlington St, Suite 6W056, Boston, MA 02116 (e-mail: dbrendaboyce@yahoo.com).

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<table>
<thead>
<tr>
<th>Reference/year</th>
<th>Type of presentation</th>
<th>No. of patients</th>
<th>Dosing protocol</th>
<th>Results</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aravanis,11 1982</td>
<td>Case study</td>
<td>3</td>
<td>7.5-10 mg/kg as a 300-mg bolus, followed by a 600-mg infusion</td>
<td>Severe local reactions occurred that included pain, redness, swelling, and acute thrombophlebitis at the site.</td>
<td>Amiodarone should be administered via a central venous catheter if possible.</td>
</tr>
<tr>
<td>Antonelli and Barzilay,12 1983</td>
<td>Descriptive study</td>
<td>33</td>
<td>2-4 mg/kg</td>
<td>24 (73%) experienced pain, redness, and swelling that was noticed a few hours after the beginning of treatment; the researchers administered 1000 international units heparin or 10 mg of hydrocortisone to the amiodarone solution. The authors noted that the addition of these drugs was ineffective in preventing phlebitis.</td>
<td>Central vein perfusion is an effective means to prevent thrombophlebitis during the administration of amiodarone.</td>
</tr>
<tr>
<td>Hilleman et al,14 1987</td>
<td>Descriptive study</td>
<td>10</td>
<td>3.8-8.7 mg/mL mean concentration</td>
<td>Phlebitis developed in 6 patients (60%).</td>
<td>Central catheter may be required if concentrations greater than 3 mg/mL must be administered.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14</td>
<td>2.5 mg/mL</td>
<td>Phlebitis developed in 1 patient.</td>
<td></td>
</tr>
<tr>
<td>Kreiss et al,15 1999</td>
<td>Descriptive study</td>
<td>20</td>
<td>Loading dose of 300 mg delivered via a peripheral catheter at a rate of 10 mg/min, followed by 900 mg delivered at a rate of 1.6 mg/min. After this 24-hour intravenous loading dose regimen, treatment was changed to an oral preparation.</td>
<td>5 patients (25%) had thrombophlebitis; the most common side effect, thrombophlebitis, in each patient was superficial, mild, and reversible.</td>
<td></td>
</tr>
<tr>
<td>Vardas et al,16 2000</td>
<td>Randomized, controlled clinical study</td>
<td>108</td>
<td>300 mg for 1 hour followed by 20 mg/kg for 24 hours</td>
<td>Phlebitis developed in 17 patients (16%) over the infusion site; amiodarone infusion was continued via a more central site.</td>
<td></td>
</tr>
<tr>
<td>Aljitawi et al,7 2005</td>
<td>Case study</td>
<td>1</td>
<td>2 mg/mL via a peripheral catheter administered at a rate of 36 mg/h</td>
<td>Initial intravenous infusion was started on hospital day 2 and discontinued when the patient’s condition was hemodynamically stable; second catheter on the opposite arm was placed when the patient’s condition once again became unstable and drug was discontinued on day 5 when erythema, warmth, and tenderness on both arms was noted.</td>
<td>Administering amiodarone via a peripheral vein may result in discomfort to patients and may extend hospitalization. Intravenous should be changed to oral amiodarone as soon as the patient’s condition allows because oral amiodarone has excellent bioavailability, is significantly less expensive than intravenous preparation, and can be safely used in stable arrhythmias.</td>
</tr>
</tbody>
</table>

Continued
nurse expert, and 8 staff nurses from various units. The tool was redesigned to incorporate the suggestions from the research council for variables not included in the original draft tool. Changes included addition of a scale for pain, documentation of additional drugs infused through the same intravenous site, and documentation to verify the use of an in-line filter. The council accepted the revised draft tool for use in the pilot test. Instructions on the use of the draft tool were printed on the back of the tool.

Pilot Testing and Revision of the Draft Tool

The draft tool was pilot tested on 3 patients by 2 members of the project team. Upon completion of the pilot test, the tool and instructions were evaluated by the project team and were revised to be more user-friendly. The revisions consisted of format changes such as font size and the layout design for the columns and lines used by data collectors to document information. The revised tool was again presented to the members of the nursing research council and was approved.

Data Collection

The final data collection tool was delivered to the critical care units where the pilot testing had

<table>
<thead>
<tr>
<th>Table 1 Continued</th>
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<tbody>
<tr>
<td>Reference/year</td>
</tr>
<tr>
<td>Slim et al.17, 2007</td>
</tr>
<tr>
<td>Halonen et al.18, 2010</td>
</tr>
<tr>
<td>Mowry and Hartman,9, 2010</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2 Phlebitis rating scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade (degree of phlebitis)</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>0+</td>
</tr>
<tr>
<td>1+</td>
</tr>
<tr>
<td>2+</td>
</tr>
<tr>
<td>3+</td>
</tr>
<tr>
<td>4+</td>
</tr>
</tbody>
</table>

been done. The units selected to participate in the project included the 3 critical care units where intravenous amiodarone is administered (progressive care, medical intensive care, and surgical intensive care). Unit-based in-service education was conducted to inform nurses of the purpose and design of the project and the use of the tool. Copies of the tool were left on each unit, and a copy of the instructions (Table 3) to guide the staff in completing the tool was posted on each unit in the medication room. For any patient receiving intravenous amiodarone, nurses were expected to record data on the collection tool every 4 hours and as necessary during administration of the drug and for 24 hours after discontinuation of amiodarone to detect any latent effects that might have occurred after the drug was stopped. Although phlebitis can occur up to 48 hours after removal of peripheral intravenous catheters, following up patients for that long was unrealistic because many were discharged from the hospital or transferred before 48 hours had elapsed.

In order to track and provide guidance and consistency in data collection, the pharmacy department notified the project coordinator once per day, via an automated system, of all patients receiving intravenous amiodarone. Members of the project team followed up each of these patients while the patients were on the unit and actively receiving intravenous amiodarone. A chart review was conducted for each patient by 2 members of the team to obtain the patient’s age, sex, and diagnosis. Further, the project team reviewed the data and filled in any missing information when possible.

### Table 3 Amiodarone intravenous (IV) site evaluation: instructions for data collection

The Nursing Research Council is evaluating the incidence of phlebitis AND pain with peripheral IV administration of amiodarone. Please evaluate your patient’s IV site in which amiodarone is infusing at least EVERY 4 hours + PRN during infusion and for 24 hours after infusion.

Data collection: June 1-November 30, 2009
- It is very important to collect the data during administration and for 24 hours after infusion.
- Monitor the site for 24 hours after IV removal or change.
- Collect data on flow sheet—keep in the blue/black med/flow sheet book.
- Use a new sheet for every peripheral IV that amiodarone runs through.
- This form is NOT part of the medical record.
- Place completed forms in the envelope in the medication room or return to Project Team, Nursing Research Council.

For questions call or page IV team.

Abbreviation: PRN, as needed.

### Table 4 Data compilation fields for each patient and occurrence of phlebitis

<table>
<thead>
<tr>
<th>Medical record number</th>
<th>Age</th>
<th>Sex</th>
<th>Service</th>
<th>Diagnosis</th>
<th>Date IV started</th>
<th>Needle gauge</th>
<th>IV site</th>
<th>Presence of phlebitis</th>
<th>Grade of phlebitis as per scale</th>
<th>Length of time IV in before amiodarone started (in hours)</th>
<th>Length of time infusion administered when phlebitis started (in hours)</th>
<th>Number of hours amiodarone infused</th>
<th>Other drugs administered via IV tubing before and/or during amiodarone</th>
<th>Comments/observations</th>
</tr>
</thead>
</table>

Abbreviation: IV, intravenous (catheter).

### Compilation of Data

Data for all patients were compiled on a single spreadsheet for analysis. Table 4 lists the categories of data for each patient and each peripheral site established for administration of amiodarone. Although patients’ identification numbers were used on this form, no names were recorded. Patients’ anonymity was maintained for all data presented here in *Critical Care Nurse*.

### Sample

Data were collected on patients with a cardiac arrhythmia in the progressive care and medical and surgical intensive care units who were starting or currently receiving amiodarone via a peripheral intravenous site. A convenience sample of 12 patients was used (Table 5). Patients received amiodarone during the months of June 2009 through
November 2009. The study was stopped after 6 months because the rate of phlebitis was higher (67%) than that reported in the current literature (7%-23%) and warranted awareness and education for nursing and medical personnel to minimize further adverse events in patients given intravenous amiodarone via a peripheral site.

### Procedure

Intravenous amiodarone was administered according to the established manufacturers’ protocols. The hospital’s pharmacy prepared the infusion solution in glass bottles. Nurses delivered the drug via an electronic infusion pump with an in-line filter on the tubing. The pump was programmed to deliver an initial bolus of 15 mg/min for 10 minutes (150 mg) and then a step-bolus dose of 1 mg/min for 6 hours (360 mg) and a maintenance dose of 0.5 mg/min for 18 hours (540 mg). Patients receiving intravenous amiodarone for more than 18 hours were given the maintenance dose until the drug was discontinued or they were changed to oral amiodarone. No other medication was administered through the intravenous catheter concurrently with amiodarone.

### Data Analysis

The data were compiled, analyzed, and interpreted by using descriptive statistics appropriate for the investigation.

### Results

Data on 12 patients with a total of 24 intravenous sites for administration of amiodarone (Table 6) were analyzed. Information not recorded on the data collection tool was gathered from review of medical records. Data for all patients were compiled on a spreadsheet and then examined. The project team examined the data for trends related to location of intravenous site, gauge of the intravenous needle used, time between establishment of the peripheral site and start of the amiodarone infusion, length of time amiodarone was administered before phlebitis developed, number of hours amiodarone was infused, and intravenous infusion of other medications before treatment with amiodarone was started.

Various grades of phlebitis developed in 8 patients (67%); 4 patients (33%) had no phlebitis (Table 7). Phlebitis developed at 12 of the 24 peripheral intravenous sites (50%). One patient had placement of an implantable cardioverter defibrillator delayed for 1 day and discharge from the hospital delayed for 1 day because of multiple incidents of phlebitis.

No association was found between the incidence or severity of phlebitis and the length of time between establishment of the peripheral intravenous site and the start of infusion of amiodarone, length of time that amiodarone was administered per catheter, length of time amiodarone was infused before phlebitis started, site of the peripheral vein selected, gauge of needle, and age or sex of the patient. No recorded information on needle gauge was available for 1 peripheral site. Two patients received magnesium sulfate intravenously through the same catheter used for amiodarone before infusion of the latter was started, but no phlebitis occurred in these patients.
No medications were delivered through the intravenous catheter during infusion of amiodarone.

Discussion

The risk for thrombophlebitis with the peripheral administration of amiodarone has been documented and continues to be an issue. Although reports suggest that phlebitis is minimized when amiodarone is administered at the recommended dosage and when an in-line filter is used, the nurses at Mount Auburn Hospital noted a high incidence of phlebitis, a finding that has been supported by our results. More recently, 1 institution has lowered the concentration of intravenous amiodarone even further, to 1.2 mg/mL, to minimize the adverse effect of phlebitis. However, further studies are needed to demonstrate the safety, efficacy, and effectiveness of this concentration in decreasing phlebitis in a larger population of patients.

According to the Infusion Nurses Society, the rate of phlebitis should be 5% or less in any given population of patients receiving peripheral infusions. However, no information indicates whether this rate includes peripheral infusion of intravenous fluids versus medications or additives. Although our sample consisted of only 12 patients, the high rate of phlebitis (67%) warrants attention. Although some researchers suggest administering amiodarone via a central catheter, this route poses risks to patients and is often not feasible in emergent situations. Even when following manufacturers’ established guidelines, nurses should not minimize the importance and necessity of keen and frequent observation of intravenous sites. Such observation is imperative to reduce patients’ risk and diminish the effects of phlebitis. Instructing patients to notify a nurse upon the first sensation of pain, tenderness, or redness may minimize undue distress. Nurses should not hesitate to immediately remove peripheral intravenous catheters at sites with signs and symptoms of phlebitis and not wait for more serious complications to occur. Diligence on the part of nurses can save a patient unnecessary discomfort and diminish the risk for interruption of treatment, prolonged care, and increased costs.

Limitations

Our study had 3 limitations. The first was the small sample size. The sample size was influenced by 2 factors: the number of appropriate patients for the project and the high proportion of patients (67%) in whom phlebitis developed. The high rate of phlebitis led us to end the study and implement practice changes to diminish the risk for further adverse events related to infusion of amiodarone.

The second limitation was the difference in the number of medical (75%) and surgical (25%) patients. At Mount Auburn Hospital, most cardiac surgical patients have a central catheter inserted before surgery, and this catheter is used to administer amiodarone postoperatively if needed.

The third limitation was lack of information on how often patients were asked if they had pain at the site when clinical signs and symptoms were not present and how quickly the nursing staff took appropriate action to discontinue the amiodarone infusion. As stated, patients’ reports of pain at the peripheral site without clinical signs or symptoms was considered an indication of phlebitis.

Conclusions

Patients who receive intravenous amiodarone via a peripheral catheter are at risk for phlebitis even when the drug is administered according to manufacturers’ protocols. The rate of phlebitis in our study was higher than rates reported in the

### Table 7

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Catheter site</th>
<th>Phlebitis rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>2+</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>3+</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>1+</td>
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<tr>
<td>5</td>
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</tr>
<tr>
<td>6</td>
<td>6</td>
<td>3+</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>1+</td>
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<tr>
<td>8</td>
<td>8</td>
<td>2+</td>
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</tr>
<tr>
<td>11</td>
<td>11</td>
<td>1+</td>
</tr>
<tr>
<td>12</td>
<td>12</td>
<td>0+</td>
</tr>
</tbody>
</table>

*a* For the purposes of this study, a 0+ was considered indicative of phlebitis. See Table 2 for rating scale.

www.ccnonline.org
Phlebitis due to infusions is a common cause of patients’ discomfort and morbidity in hospitals. Although Hilleman et al and the Infusion Nurses Society agree that risk for phlebitis has many factors, including the size of the cannula used, the patient’s age and degree of illness, prescription properties (eg pH and osmolarity of the infusion solution and the rate of infusion), duration of therapy, frequent handling of the infusion delivery system, infusion history, and skill of clinicians (insertion technique and care and maintenance practices), we found no association between these factors and development of phlebitis. Although we focused on patients receiving intravenous amiodarone via a peripheral site, caregivers need to recognize that phlebitis associated with an infusion may not be due to just a single risk factor.

Implications for Nursing Practice

On the basis of our results, numerous practice changes are indicated. At Mount Auburn Hospital, intravenous therapy nurses are not routinely involved in insertion or maintenance of intravenous catheters in the intensive care units selected for our study. As specialists in the insertion, assessment, and care of intravenous catheters, intravenous therapy nurses monitor patients receiving intravenous amiodarone. Further, staff nurses currently do not participate in any competency testing related to infusion of intravenous amiodarone. A competency test should be developed in which all nurses must demonstrate skill and knowledge in the administration of intravenous medications, including amiodarone, once per year.

Critical care nurses should thoughtfully consider the protocols for administering intravenous amiodarone and the nursing assessment and care required. Adverse events can be decreased if nurses involved with peripheral administration of intravenous amiodarone have sufficient education on the risks of phlebitis, a solid understanding of the importance of frequent assessment and documentation of intravenous sites, the determination to change the intravenous site upon the first sign or symptom of phlebitis, and awareness that an in-line filter must be used for administration of amiodarone. Cardiologists, emergency room physicians, and intensivists should be reminded of the high risk for phlebitis in patients receiving intravenous amiodarone and the harmful effects the complication can have on both patients and the health care system.


References


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