A multiple case study examining the risk factors contributing to Amiodarone infusion related phlebitis in a New Zealand cardiac care centre

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Abstract

Aim: This study aimed to investigate amiodarone infusion related phlebitis in a local cardiac centre in a large metropolitan hospital within Te Whatu Ora- Health New Zealand, focusing on assessing its incidence, identifying contributing factors, evaluating treatment practices and uncovering policy gaps.

Background: In hospitals, amiodarone, a widely used antiarrhythmic drug, is mostly administered intravenously via peripheral catheters. However, the incidence of amiodarone infusion related phlebitis, which may lead to severe complications, still needs to be studied more in the context of New Zealand healthcare.

Methods: Yin's case analysis methodology was used to analyse two cases: a seven- year clinical audit from March 2016 to June 2023 in the local cardiac centre and four local policies. Cross case analysis examined the two cases using triangulation to determine the gaps between practice reality and policy and to discover how and why amiodarone infusions occur.

Results: The incidence of amiodarone infusion related phlebitis was 8.4%. Contributing factors revealed that intravenous catheter locations were predominantly in the antecubital fossa (63%), and participants had a size 20 or larger cannula in situ (90%). There was a lack of use of the visual infusion phlebitis scores for assessment. Other findings revealed that 45% of phlebitis cases occurred during the amiodarone infusion, and 55% occurred after infusion. Seventy percent of the patients were seen by a doctor and 54% were charted oral antibiotics as treatment.

Conclusion: To improve patient outcomes and align with best evidenced guidelines, it is recommended that local policies are updated to address the identified gaps. There is a need to promote nurses' awareness of amiodarone related phlebitis prevention, especially in relation to which site and gauge cannula should be used, increasing assessment frequency and scoring to assess phlebitis severity. There is a need for monitoring post infusion, alternating warm and cold compresses and arranging timely medical reviews. Other recommendations include using dedicated IV cannulas and inline filters for continuous amiodarone infusions.

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AIRP	amiodarone infusion related phlebitis
PIVC	peripheral intravenous catheter
AAD	antiarrhythmic drug
AF	atrial fibrillation
IV	intravenous
CVC	central venous catheter
INS	Infusion Nurse Society
CYP	Cytochrome
VIP	Visual infusion phlebitis
CINAHL	Cumulative Index to Nursing and Allied Health Literature
HABSI	healthcare associated bloodstream infections
M.C.S.	microbiology, culture and sensitivity
ACF	antecubital fossa
NZ	New Zealand
DHB	District Health Board
AV	atrioventricular

Attestation of authorship

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning.

28/10/2023

Signature Date

Chapter 1 Introduction and overview

This chapter introduces amiodarone infusion-related phlebitis and its prevalence as a common complication of peripheral intravenous catheters (PIVCs). It introduces the research questions, provides an overview of the thesis structure, and highlights the pivotal role of nurses in managing PIVCs.

1.1 Background

Amiodarone is an important antiarrhythmic drug (AAD) commonly used for the treatment of supraventricular and ventricular arrhythmias, including atrial fibrillation (AF), atrial flutter, supraventricular and ventricular tachycardia and ventricular fibrillation (Auer et al., 2002; Camm et al., 2011; New Zealand Medsafe, 2022; Pannone et al., 2021). In the New Zealand hospital setting, when delivered intravenously, amiodarone is supplied in ampoules of 150mg in a 3 mL solution. It can be given by direct intravenous (IV) injection in clinical emergencies, intermittent infusion for loading and subsequent doses, or continuous infusion (New Zealand Hospital Pharmacists' Association Inc., 2023). To avoid peripherally infused amiodarone related phlebitis, it is recommended that a central venous catheter (CVC) must be used when the concentration exceeds 2mg/mL and is preferred for repeated and continuous infusions (New Zealand Hospital Pharmacists' Association Inc., 2023).

In practice reality, however, peripheral intravenous catheters (PIVCs) are most frequently used for amiodarone infusions. This is because CVC insertion is more complicated, requiring specially trained people in a sterile environment (Tse & Schick, 2022). PIVC insertions are easier and quicker, especially in emergencies of new uncontrolled AF or during an electrical storm when there is a lack of time to place a

CVC (Hannibal et al., 2016). In preventing AF post cardiac surgery, amiodarone infusion is short-term, so CVC is not usually required (Boyce & Yee, 2012; Murphy et al., 2020). Besides, CVC has the risk of complications, such as pneumothorax, arrhythmias, hematoma, and bloodstream infections, leading to consequent morbidity, mortality and increased hospital costs (Chopra, 2012, as cited in Oragano et al., 2019).

Peripheral vein catheters also have risks, with phlebitis being the most prominent. Phlebitis is the inflammation of the tunica intima, the inner wall of the vein, which is preventable. The signs and symptoms of phlebitis include the cardinal signs of inflammation: “pain, tenderness, swelling, redness, skin hot to touch and the presence of a palpable cord” (Infusion Nurse Society, 2021, p. 138).

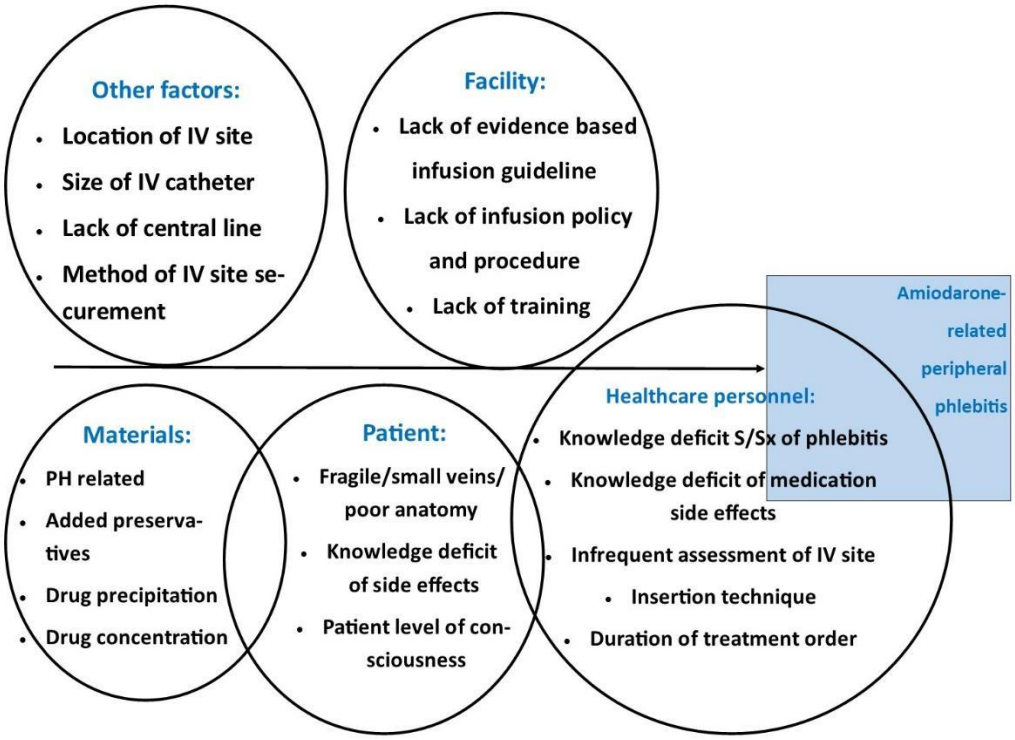
Phlebitis has harmful impacts on patients and the healthcare system. It can lead to patient pain, discomfort, and loss of future venous access (Hannibal, 2016; Macklin, 2003; Norton et al., 2013). It may also lead to further infection, untreated bacterial phlebitis or catheter-related bloodstream infection, which may eventually cause sepsis or infective endocarditis (Habib et al., 2015, as cited in Brors et al., 2023). A rare complication is also necrosis, which was noted by Simoni et al. (2011). Amiodarone infusion related phlebitis (AIRP) also impacts the health service budget, for example, the need for multiple PIVC placement costs and an increase in days spent in the hospital (Malachs et al., 2006). Boyce and Yee (2012) found that hospital stays increased by one day, whereas Slim et al. (2007) found an increase of six days.

The rate of amiodarone related phlebitis varies. The Infusion Nurse Society (INS) benchmark rate is 5% (2007). However, practice reality is significantly higher. In a systematic review, phlebitis rates were reported, ranging anywhere from 36% to 85%,

while in other studies, the rate was lower, ranging from 0% to 27% (Oragano et al., 2019). The disparity may be attributed to various factors, for example, differences in sampling, methods, and practice standards of the healthcare settings (Oragano et al., 2019). The causes of AIRP are numerous; Mindo (2018) summarised the possible causes of the high incidence of AIRP in a cardiac-focused ward and placed these under five major categories: the facility, the patient, materials, healthcare personnel and other factors (see Figure 1).

Figure 1.

Factors contributing to the development of high incidence of amiodarone-related peripheral phlebitis in a cardiac-focused ward



(Diagram adapted from Mindo, 2018, p.28)

One of the prominent reasons that amiodarone is at high risk for phlebitis is its high acidic pH range (3.5-4.5); this acidy predisposes the vein intima to damage (Ward &

Yalkowsky, 1993). Precipitation and crystallisation during administration can irritate the delicate endothelium with crystal formation acting as sharp needles that stick to the vein intima (Ward & Yalkowsky, 1993). Another cause of chemical irritation is that the stabilisers and preservatives for compounding amiodarone into the IV infusion work as irritants (Spiering, 2014). Literature also suggested that different amiodarone infusion rates, total dose, duration, and concentration can affect phlebitis rates. For example, longer continuous infusions caused more phlebitis than bolus infusions (Oragano et al., 2019). Norton et al. (2013) found that phlebitis rates increased with total doses reaching 3g. The inverse is also the case with Hilleman and Hansen (1987) and Mowry and Harman (2011), noting that phlebitis rates reduced with decreased concentration.

Nursing practice is a contributing factor to AIRP. The location of the IV insertion site, choice of PIVC size, and methods of IV site securement can make significant differences in outcomes (Milutinovic et al., 2015). Spiering (2014) reported that a small PIVC placed in a large vein resulted in the lowest phlebitis rate because of increased dilution of acidic infusion in the blood. It was also found that injection site splinting reduces AIRP in a randomized clinical trial (Ayat-Isfahani et al., 2017). Murphy et al. (2020) implemented evidenced-based guidelines to decrease AIRP and improve early detection of phlebitis, including increased assessment frequency of PIVC, criteria of vein selection, and utilisation of a standardised grading tool for assessment. There was a 48% phlebitis case reduction during the six months post the intervention in this study.

1.2 Aim of study and research question

This thesis aims to gain insights into the causes of Amiodarone infusion related phlebitis (AIRP) in a cardiac centre in a large public metropolitan hospital within Te Whatu Ora-Health, New Zealand. By discovering the causes that lead to amiodarone phlebitis and what the best practice for phlebitis treatment is, this thesis aims to make practice change recommendations and improve the quality of care. The following research questions guided this inquiry:

1. How does the incidence of AIRP compare in the cardiac centre being examined to global incidence?
2. Why are patients receiving amiodarone infusion via a peripheral intravenous catheter at risk for developing phlebitis?
3. How are AIRP treated in the cardiac centre?
4. What and why are there gaps between local policies and best evidenced guidelines?

1.3 Chapter overview

Chapter One: This introductory chapter highlighted why peripheral intravenous amiodarone infusions lead to phlebitis and how this impacts patients. It stressed the prevalence of phlebitis as a common PIVC complication and emphasised the role of nurses in PIVC management. The chapter outlined the research questions that will guide the study and presented an overview of the thesis structure.

Chapter Two: This chapter is a more in-depth literature review. This chapter defines what amiodarone is, what it is used for, and how it is administered. It also explores the literature on what is currently known about amiodarone infusion related phlebitis

(AIRP). A few themes are discussed to develop the background and support understanding of the contributing factors of AIRP and its treatment.

Chapter Three: This chapter discusses the methodology. Yin's multiple case study method and design are followed to examine how and why AIRP occurred in the context of the local cardiac centre. This chapter elaborates the research questions, rationales, context of the case study, philosophical underpinnings, and data collection and analysis. The ethical considerations for the undertaking of the study are also outlined.

Chapter Four: This chapter presents the findings of two cases: a clinical audit of amiodarone infusion-related phlebitis over seven years from March 31, 2016, to June 12, 2023, in the examined cardiac centre. The second case is presented, a summary review of local policies and document analysis of important contributing factors of AIRP in the local context. Triangulation of these two cases is also presented.

Chapter Five: This final chapter discusses the findings and compares these findings to the broader literature on the topic. This chapter also includes the research's strengths, limitations, implications for practice recommendations and the conclusion.

Chapter 2 Literature review

This chapter explores amiodarone in more detail, including the history of amiodarone, pharmacotherapeutics, pharmacodynamics and pharmacokinetics. This review includes a modified integrative review that sought to explore the literature on what is currently known about amiodarone infusion related peripheral IV phlebitis (AIRP). Nine themes are presented from the findings of the integrative review and help support an understanding of the contributing factors of AIRP and its treatment.

2.1 Amiodarone

2.1.1 History of amiodarone

Amiodarone is an antiarrhythmic drug derived from the plant Ammi visnaga. The plant was known as a useful medicinal herb in various cultures from ancient and medieval times (Khalil et al., 2020). Traditionally, extraction of plant materials was done by boiling its dried seeds in water or tincture of its fruits. In the late 1800s and early 1900s, Egyptian clinicians extracted crystalline substances from Ammi visnaga, of which Khellin was the most active compound and found to have muscle relaxant activity on all smooth muscles and a mild diuretic effect (Tavolinejad et al., 2019).

Later, Khellin was experimented with as a coronary vasodilator for treating angina. Compared with other anti-anginal agents, such as nitrates, Khellin had a significant benefit for its selectivity for coronary arteries; therefore, it does not cause systemic vasodilation or blood pressure drop. In the 1960s, the Labaz group in Belgium synthesised amiodarone based on the benzofuran portion of Khellin (Tavolinejad et al., 2019).

Amiodarone's antiarrhythmic effect was tested on animals in 1969, and it was hypothesised that it could be a strong AAD (antiarrhythmic drug) due to its effect on cardiac action potential (Tavolinejad et al., 2019). After clinical experiments of oral and IV amiodarone in the 1970s, there was expanding evidence of its mechanism of action and increasing use in practice. By 1980, amiodarone was commonly used in Europe for treating arrhythmias (Tavolinejad et al., 2019). In 1985, it was approved as an AAD by the US Food and Drug Administration and remains the main drug for treating antiarrhythmias today (Tavolinejad et al., 2019).

2.1.2 Pharmacotherapeutics

Amiodarone injection is a solution of amiodarone hydrochloride, an antiarrhythmic drug given intravenously (New Zealand Medsafe, 2022). Intravenous amiodarone is preferred when treating and preventing life-threatening arrhythmias refractory to other therapies or when oral amiodarone is not tolerated (Biancatelli et al., 2019). Amiodarone has four main clinical indications. Firstly, it has an important role in the acute management of ventricular tachyarrhythmias, regardless of hemodynamic stability (Vsaallo & Trohman, 2007). Secondly, it is a first-line effective treatment of atrial fibrillation in patients with heart failure (Levy, 1994). Thirdly, it prevents atrial or ventricular arrhythmias perioperatively of cardiac surgery (Atreya et al., 2019). Finally, amiodarone is used as an adjunct to implantable cardioverter-defibrillator therapy to decrease the number of shocks needed in resuscitation (Mujovic et al., 2020).

2.1.3 Pharmacodynamics of amiodarone

Amiodarone, an iodinated benzofuran derivative, has two iodine molecules, making up 37.5% of the drug's weight (Biancatelli et al., 2019; Pannone et al., 2021; Podrid,

1995). Its structural similarity to thyroid hormones results in the release of over 10% free iodine in vivo, contributing to its anti-thyroid effect (Nademanee et al., 1986, as cited in Medic et al., 2022).

Amiodarone belongs to Vaughan Williams Class III AAD (antiarrhythmic drug) but shows electrophysiological characteristics of all four Vaughan Williams classes (Martino et al., 2001). Its primary Class III effect prolongs cardiac action potential and repolarisation by inhibiting potassium ion flux during phases 2 and 3, increasing refractory periods, reducing membrane excitability, and mitigating arrhythmias (Pannone et al., 2021). Amiodarone differs from other Class III drugs by prolonging repolarisation at higher heart rates (Anderson et al., 1989).

As mentioned above, amiodarone shows electrophysiological characteristics of four Vaughan Williams classes; it emulates Class I activity, which occurs primarily during tachycardia, slowing the upstroke of action potentials and depressing sinus and atrioventricular (AV) node automaticity (Mason et al., 1983). Class II effects inhibit alpha and beta-adrenergic receptors noncompetitively and reduce beta-adrenergic receptor numbers (Venkatesh et al., 1986). Its Class IV action is where amiodarone blocks L-type calcium and myocardial potassium channels, negatively impacting nodal tissues' conduction and refractoriness in the sinus and AV nodes (Biancatelli et al., 2019). Amiodarone prolongs cardiac action potential phases II and III, myocyte repolarisation, and refractory periods, with limited effects on the bundle of His and purkinje fibres (Pannone et al., 2021).

Amiodarone has significant hemodynamic effects, dilating coronary arteries and increasing coronary blood supply, reducing systemic blood pressure and afterload, and

displaying mild negative inotropic actions offset by peripheral vascular effects (Bertholet et al., 1983). Its use as an anti-anginal agent stems from its vasodilatory properties, mediated by various pathways, including cyclooxygenase, nitric oxide synthase activation, and alpha-adrenergic receptor blockade (Pannone et al., 2021).

Amiodarone injection can cause severe and potentially fatal side effects, such as pulmonary toxicity, hepatic injury, cardiac arrhythmias, hypotension, bradycardia, thyroid dysfunction, and neurological effects. Patients should be closely monitored for signs and symptoms of these adverse reactions, and the dose should be adjusted or discontinued as needed (Biancatelli et al., 2019).

2.1.4 Pharmacokinetics of amiodarone

The intravenous formulation ensures complete bioavailability compared to the oral form. Oral amiodarone has slow and incomplete gastrointestinal absorption, with approximately 50% bioavailability due to hepatic metabolism, first-pass intestinal mucosal effects, and incomplete absorption (Medic et al., 2022). The bioavailability can also be influenced by factors such as age, liver disease, and interactions with other drugs affecting cytochrome (CYP) 450 enzymes, essential for amiodarone metabolism (Biancatelli et al., 2019). Therefore, the drug's onset of action is delayed, requiring a long loading period (up to 3 months) before antiarrhythmic effects become apparent, and the loading duration and optimal dose vary among patients (Medic et al., 2022).

A peak serum level is achieved 3 to 7 hours after oral administration. Plasma levels increase with dose, as they are approximately dose proportional (Hrudikova et al., 2017). Amiodarone is highly lipophilic and binds extensively to proteins and lipids. It has a large volume of distribution (50L) and accumulates mainly in adipose tissue,

slowly releasing to well-perfused organs, such as the liver, lungs and skin. Hepatic metabolism, primarily by the enzyme CYP3A4, produces the principal metabolite, desethyl-amiodarone (Medic et al., 2022). Drug metabolism is sensitive to cytochromes inhibitors (e.g. grapefruit juice, ketoconazole, clarithromycin, HIV protease inhibitors, and hepatitis C virus medication sofosbuvir) and inducers (e.g., rifampicin, phenobarbital, phenytoin, carbamazepine, nevirapine, efavirenz and pioglitzone), affecting drug efficacy (Pannone et al., 2021). The elimination half-life differs individually but is typically long, ranging from 16 to 190 days, due to extensive storage and binding to adipose tissue (Podrid, 1995).

2.2 Phlebitis

2.2.1 Pathophysiology; physical, chemical and infective phlebitis

Phlebitis is one of the major risks of amiodarone infusions and is the inflammation of the inner wall of the vein. The inside wall of a vein is mainly made of endothelial cells, which hold the vein together. When damaged or irritated, they release chemicals, such as histamines, bradykinin and serotonin, which trigger a pain response and vasodilation, with more blood going to the area (Macklin, 2003). The blood vessels also become leaky, so fluids and proteins enter the surrounding interstitial space, causing swelling and pain (Macklin, 2003). Procoagulant factors in the endothelial lining activate the clotting cascade, releasing leukocytes gathered at the injury location, releasing pyrogens, stimulating the hypothalamus, and raising body temperature. A clot can form in the vein if the irritation persists and is not removed or treated. As the inflammation goes on, there will be more swelling and stiffness or the presence of a hardened vein called a cord (Macklin, 2003). Thrombophlebitis is phlebitis that occurs

alongside the forming of a blood clot within a superficial vein, accompanied by an inflammatory response affecting the vein wall and the surrounding tissues (Sobreira et al., 2008).

Phlebitis has three broad causes: physical, chemical, and infective. The rubbing motion and positioning of PIVC within the vein wall cause physical or mechanical phlebitis. The intravenous catheters' tip can move more if it is near a joint, a vein valve or a visible venous bifurcation or if the PIVC is not well attached to the skin (Marsh, 2019). Besides the location, another contributing factor is the physical feature of the catheter; bigger or stiffer catheters can increase the phlebitis risk, while longer and softer catheters decrease the risk by reducing friction (Marsh, 2019). PIVC insertion can also lead to physical phlebitis, with factors such as prolonged insertion time, repositioning or manipulating the IV cannula during the puncture or after inserting it into the skin and subcutaneous tissue (Buzatto et al., 2016). Rushing PIVC insertion in emergency cardiac arrhythmias can also increase phlebitis due to intimal damage and vein tearing (Oregano et al., 2019).

Chemical phlebitis is due to IV drugs or fluids irritating the vein wall. When substances are too basic or acidic, the change in normal blood pH or osmolality can irritate the vein, especially when the PIVC site is a small vein with insufficient blood flow or the drug is under-diluted or given too fast (McCallum & Higgins, 2012). Symptoms usually appear along or above the PIVC tip and can cause a swollen superficial vein or a palpable cord (Macklin, 2003).

Infective phlebitis is due to irritation of the vein wall "when micro-organisms track along the insertion site and into the catheterised vein" (Marsh, 2019, p.28). Causes

often involve a breach in the aseptic technique when inserting or maintaining PIVCs. Bacteria proliferate in biofilm formation as gems colonising at the internal or external PIVC surface, thus starting a local phlebitis reaction or increasing the risk of catheter-related bloodstream infection (Higginson & Parry, 2011).

2.2.2 Phlebitis assessment: the Visual infusion phlebitis (VIP) score system

A Visual infusion phlebitis (VIP) score system is recommended to assess phlebitis. The VIP system can help accurately assess phlebitis severity, ensuring consistency in assessment and communication among healthcare professionals (Ray-Barruel et al., 2014). Early detection and addressing the problem can reduce the risk of complications and improve patient outcomes (Murphy et al., 2020). In the organisation being examined, the VIP is utilised for assessment (see Figure 2). The VIP has five severity scales ranging from 0 = (No sign of phlebitis) to 5 = (Advanced stage of thrombophlebitis) and also comes with corresponding interventions. However, the VIP is only one of the 71 phlebitis scales that exist and has not undergone rigorous testing for reliability, so the score may vary depending on who or how it is used and may not reflect true or severe phlebitis (Ray-Barruel et al., 2014).

Figure 2

Visual Infusion Phlebitis assessment score system

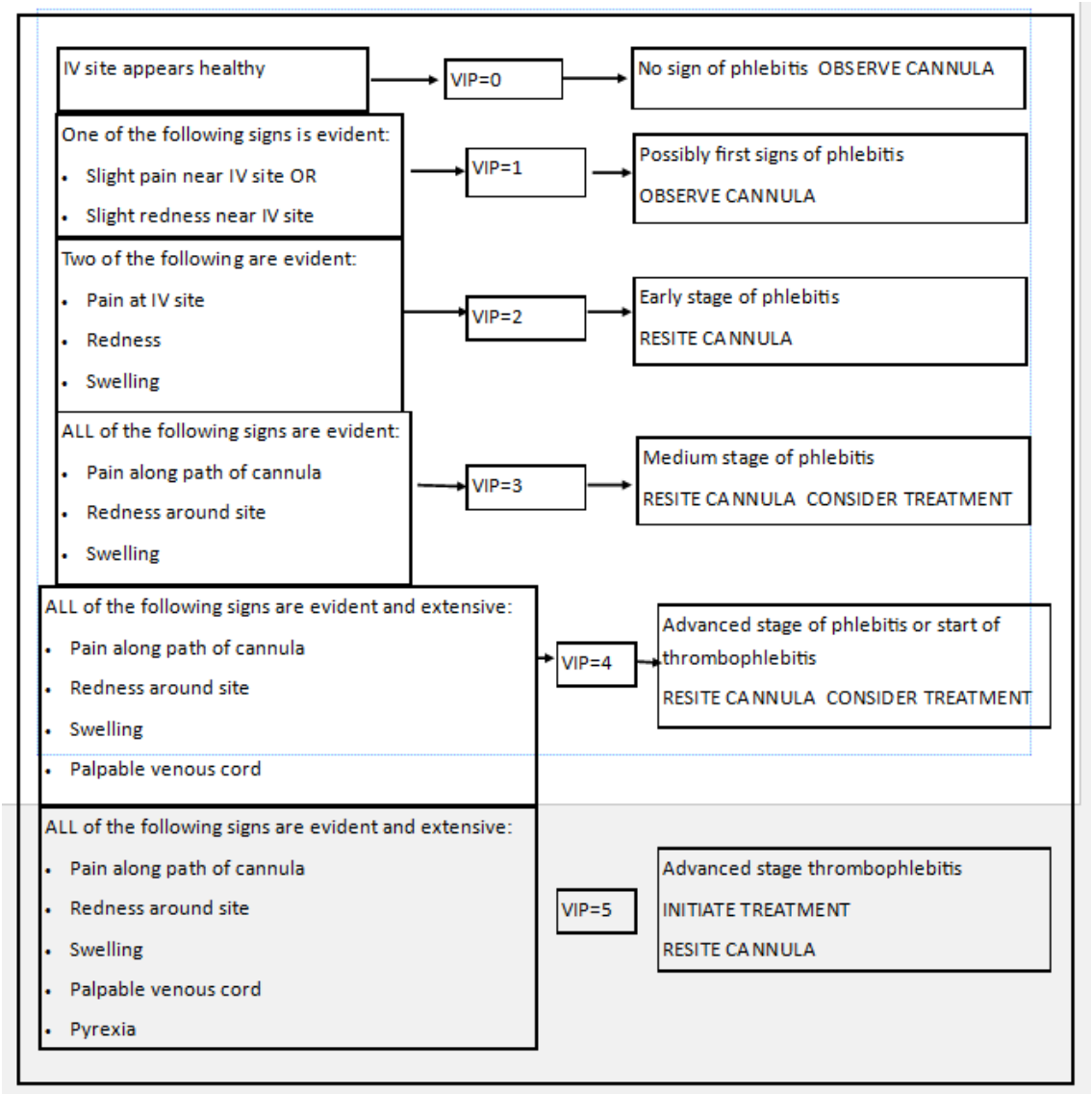


Diagram adapted from Te Whatu Ora Waitemata, 2023, p. 8

2.3 Literature search looking at reasons contributing to AIRP

This next section is a comprehensive and systematic literature review to assess what is being suggested globally in the prevention of AIRP. This review includes a two-phase systematic search. Phase one involved a database search including Cumulative Index to Nursing and Allied Health Literature (CINAHL) Complete, MEDLINE (Medical Literature On-Line), Scopus and Google Scholar to look for peer reviewed articles. The second

phase of the search focused on amiodarone policies, pharmaceutical guidelines and phlebitis treatment using a Google search.

2.3.1 Database search

Search terms and keywords included amiodarone, amiodarone infusion, intravenous amiodarone, phlebitis, peripheral catheter, extended to amiodarone extravasation, and nursing guidelines, best practices. In CINAHL Complete and MEDLINE, 57 articles were found; In Scopus, 135 articles were found; Google Scholar yielded 1660 results, and the first 100 were reviewed. Limits were then applied according to inclusion criteria (see Table 1). Duplicates were excluded, which yielded 37 relevant articles. After titles and article abstracts were scanned, 18 articles were eventually selected (See Appendix A for the title, author and type of article reviewed).

Table 1.

Inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
Full text	Duplicates
English language	Articles not in English
Peer reviewed journal articles	Non peer reviewed articles
Published between 2007 and 2023 (the search covers 15 years due to scarcity of literature on the AIRP topic)	Articles older than 15 years
Research about humans and adults 18 years and older	Those under the age of 18
Relevant to the topics: risk factors related to AIRP and amiodarone Infusion practices related to AIRP or phlebitis reduction as the primary outcome	Non related to AIRP

2.3.2 Guideline search

The second part of the integrative review was to review local and international policies. A Google search found ten guidelines, including four from New Zealand, two from Australia, two from England and two from the USA. (See Appendix B).

Thematic analysis was used to identify and examine themes within the selected literature and policies. Firstly, a thorough data familiarisation phase was achieved by reading the articles thoroughly (Clarke & Braun, 2013). The coding processes started as specific concepts and ideas were extracted from the texts. This required looking closely into the articles to seek common themes, such as repeated ideas, topics, or methods of putting things (Clarke & Braun, 2013). As the analysis progressed, these codes were systematically organized into potential themes, with a search for recurring patterns and connections across the literature (Clarke & Braun, 2013). Finally, the themes were reported with supporting evidence from the literature. It is a critical survey and assessment of the existing research on the thesis topic (Clarke & Braun, 2013).

2.4 Overview of Themes

2.4.1 Theme 1 Inline filter

An inline filter is commonly recommended during IV amiodarone infusion to prevent phlebitis, especially in high-concentration regimes. According to various sources, this practice effectively reduces AIRP (New Zealand Hospital Pharmacists' Association Inc., 2023; New Zealand Medsafe, 2023; Hannibal, 2016; Oragano et al., 2019; Seeney, 2019; Slim et al., 2007). Using an inline filter is believed to protect against amiodarone

crystallisation and can help reduce the rate and severity of phlebitis (Oragano et al., 2019). Additionally, the inline filter is effective in removing contaminants from infusion fluids, such as particulates, bacteria, endotoxins, precipitates, large lipids, and air, which can lead to inflammation (Friedland 1985, as cited in Niel-Weise et al., 2010). Therefore, the inline filter is widely implemented in amiodarone infusion policies in many hospitals worldwide.

On the other hand, using an inline filter for reducing amiodarone infusion related phlebitis remains controversial. The Infusion Nurse Society (2016) stated a lack of evidence to support routine inline filter use, except for human blood components (as cited in Hannibal, 2016). A meta-analysis of randomised control trials concluded that routine use of inline filters in peripheral IV catheters cannot be recommended as there is no clear evidence of their benefits (Niel-Weise et al., 2010). However, Spiering (2014) believed that an inline filter should still be used because trials in Niel-Weises' meta-analysis were unrelated to IV amiodarone infusion.

Hannibal (2016) argues that it is unclear what type and size of filter, or if any, aids in AIRP prevention in their research to test out inline filter effectiveness. In Thailand, Cheewatanakornkul et al. (2022) concluded that the high concentration caused a higher phlebitis rate despite using an inline filter. Cheewatanakornkul et al. (2022) used an inline filter for amiodarone infusion with a filter media of 0.2 micromillimetres and a positively charged Nylon Posidyne membrane. They analysed 214 cases of amiodarone infusion by comparing high-concentration IV amiodarone 2mg/mL infusion with an inline filter and low concentration 1.5mg/mL infusion without an inline filter. However, the research design was flawed because high-risk patients, such as older adults, patients with difficulty in vein access for cannulation, prolonged

amiodarone infusion, and low-risk patient groups, were not separated (Cheewatanakornkul et al., 2022).

It is rationalised that an inline filter may not be effective based on the theory that dilution and mixing of amiodarone within the bloodstream during administration can lead to crystallisation if its solubility limits are approached. Norton et al. (2013) argued that an inline filter will be ineffective if amiodarone precipitates upon contacting blood at the catheter site. Norton et al. (2013) further explained that precipitation within the vessel was dependent on the ratio of the injection rate to the blood flow rate despite implementing a filter.

Using an inline filter for high-concentration infusions is not as effective for preventing AIRP as recommended by manufacturers. While manufacturers reported that phlebitis happened at doses greater than 3 mg/mL, the complication could be minimised by using a more dilute concentration of 2.5 mg/mL and inline filters (as cited in Boyce & Yee, 2012).

To conclude, no evidence exists that an inline filter can eliminate phlebitis during amiodarone infusions. An inline filter is only one component of the prevention bundle.

2.4.2 Theme 2 IV cannula site, size and insertion technique

Inserting the smallest catheter into the largest vein can reduce amiodarone infusion related phlebitis. To avoid tissue damage during peripheral infusion, it is suggested that the selected vein should be large and intact with good flow return; the rationale is due to better haemodilution of acidic drug solution in large veins (Gorski et al., 2015; Spiering, 2014; Yalkowsky et al., 1998). It is best to avoid inserting a large PIVC into a small vein, which can lead to localised trauma. A larger gauge catheter leaves less

buffer room between the PIVC and the vein wall, increasing the risk of mechanical phlebitis (Macklin, 2003, as cited in Marsh, 2019). Therefore, some clinical practice guidelines specify that a small size gauge 22 is preferred, and the forearm should be the preferred site for peripheral amiodarone infusion (Brors et al., 2023; Macklin, 2003). Therefore, a bigger vein and smaller cannula should be an agreed basic principle in amiodarone infusion practice.

In addition, peripheral intravenous catheters should not be placed in flexion or high mobility areas. Several studies indicate that traumatic phlebitis is significantly associated with PIVC located in the elbow/ antecubital fossa region (Brors et al., 2023; Buzatto et al., 2016; Kalkan Ugurlu & Enc, 2022). Ayat-Isfahani et al. (2017) suggest that catheter size is not an important contributing factor. However, the catheter movement associated with bending and straightening the arm is the major cause of mechanical phlebitis. Butler et al. (2021) proposed that a peripheral infusion location should be chosen in the following preferred order: forearm (basilica, cephalic and median antebrachial), dorsum of hand, wrist and antecubital fossa. Consequently, the elbow/antecubital region should be the last choice when inserting a catheter.

Another significant aspect of research findings is that nurses do not always follow the amiodarone infusion clinical practice guidelines when choosing a site, size and insertion technique. Brors et al. (2023) found inconsistencies between practice reality and guidelines, as antecubital was the most common PIVC site, and bigger cannulas (18 gauge) were mostly used in a large university hospital in Norway. There was confusion among nurses about the best anatomical placement of PIVCs because some literature reported forearm insertion having a risk of developing infusion phlebitis. However, the local practice guideline states to choose the forearm first. For example,

Buzatto et al. (2016) found increased AIRP in forearm puncture sites, but the forearm, although where most of the PIVCs were inserted, was not statistically significant compared to other puncture sites. Such a discrepancy could result in less trust in guidelines from the nursing perspective and become a barrier to implementation (Brors et al., 2023). It is important to educate nurses about the impact of AIRP on patients and reduce the nursing knowledge gap.

Intravenous cannula insertion is an influential factor in phlebitis development. Rushed PIVC insertion in emergency cardiac arrhythmias can increase phlebitis rates due to intimal damage and vein tearing (Oregano et al., 2019). Insertion technique can be another contributor. It is not optimal practice when prolonged IV cannula repositioning is required to go into the vein once it enters the skin and subcutaneous tissue (Buzatto et al., 2016; Tinoco et al., 2014). As nurses have various cannulation skills, one recommended strategy for reducing AIPR is to develop an IV therapy nurse specialist in inserting and monitoring of IV catheters for patients receiving IV amiodarone (Boyce & Yee, 2012). There are many factors to consider, especially when nurses are heavily involved in the cannulation process.

2.4.3 Theme 3 Amiodarone drug concentration

The infusion policy on drug concentration varies significantly in the literature depending on the local protocol. In most articles, the mainstream infusion practice is divided into three steps. An initial bolus dose of 1.5mg/mL was delivered at a rate of 15mg/min infused for 10 minutes (total dose 150mg). This infusion is followed by a step-bolus of 1.8 mg/mL delivered at a rate of 1mg/min for 6 hours (total dose 360mg) and a maintenance dose of 0.5 mg/min for 18 hours (total dose 540mg) (Boyce & Yee, 2012; Bagheri-Nesami et al., 2015; Buzatto et al., 2016; Florek et al., 2023; Hannibal,

2016; Siddoway, 2003). Baxter Inc. America made pre-mixed injection bags branded Nexterone, ready to use, minimising mixing/compound errors in urgent situations (Baxter, 2023). The concentrations are 150mg/100mLs of Dextrose 5% and 360mg in 200mLs.

In contrast to stepwise dosing, the weight-based drug dosing was prevalent in some other countries, including New Zealand: 5mg/kg for a loading dose with a maximum of 300mg and 10-20 mg/kg for a continuous dose with a maximum of 900mg (Grampians Health Ballarat, 2021; New Zealand Hospital Pharmacists' Association Inc., 2023; NHS Gloucestershire Hospitals, 2021; Te Whatu Ora Waitemata, 2020; The Royal Hospital for Women, 2018; Wanganui Hospital, n.d.).

The solution concentration for IV infusion ranges from 1 to 6 mg/mL (Tinoco et al., 2014). Some local hospital policies require 3mg/mL for a bolus dose over 10-30 minutes (Ayat-Isfahani et al., 2017). A higher concentration is needed for specific patients, such as those with heart failure and who are on fluid restrictions, those with renal failure, and those with clinical fluid overload (Cheewatanakornkul et al., 2022).

It has been commonly believed that lower amiodarone infusion concentration is related to a lower phlebitis rate. Hilleman et al. (1987) and Mowry and Hartman (2011) found that the phlebitis rate decreased when the amiodarone concentration decreased (as cited in Oragano et al., 2019). However, there is a balance between drug efficacy and concentration. Oragano et al. (2019) mentioned that further studies are required to demonstrate amiodarone concentration's safety, efficacy, and effectiveness in reducing AIRP in a bigger patient population. Nurses usually follow local pharmacy guidelines during administration and have little control over this factor.

There has yet to be a consensus regarding the safe amiodarone infusion concentration range in the literature. Most infusion guidelines worldwide state a maximum of 2mg/mL for peripheral infusion and CVC for higher concentration and repeated or continuous infusions (Cheewatanakornkul et al., 2022; Martinho & Rodrigues, 2008; Te Whatu Ora Waitemata, 2020; Tinoco et al., 2014). Buzatto et al. (2016) found that phlebitis incidence may get up to 55% when amiodarone is given via a PIVC in a concentration greater than 3mg/mL for over one hour; however, his sample included 102 older adults only. Cheewatanakornkul et al. (2022) recommended 1.5 mg/mL as a safe concentration for PIVC infusion. Slim et al. (2007) found that even concentrations of 1.8 mg/mL caused phlebitis. Similarly, Oragano et al. (2019) stated that increasing the infusion concentration from 1.2mg/mL to 1.8mg/mL increased phlebitis rates.

Thus far, this section has reviewed the amiodarone infusion concentration range globally. Lower amiodarone infusion concentrations are associated with reduced phlebitis rates, but the balance between drug efficacy and concentration is crucial.

2.4.4 Theme 4 IV cannula maintenance and care

More intensive and precise monitoring during intravenous treatment with amiodarone can help reduce phlebitis. Frequent assessment and early recognition of painful PIVC sites can increase prompt treatment, therefore reducing harm and discomfort. It is more important for older patients and females, according to Buzatto et al. (2016). The literature offers varying recommendations, advocating for assessments and documentation occurring every 1 to 4 hours during the infusion or at 4-hour intervals post-infusion and/or IV catheter removal (Cottrill, 2022; Murphy et al., 2020; Norton et al., 2013; Tinoco et al., 2014; Woods et al., 2022). Assessment includes visual checking and palpation around the PIVC site. Nurses must stop the infusion at the first sight of

phlebitis and change the infusion to the other unaffected arm (Murphy et al., 2020). Assessing PIVC more frequently during amiodarone infusion is important to prevent phlebitis.

Peripheral intravenous catheter securement practice is also a contributing factor. Fixation of the injection site using fiberglass close brace to secure PIVC significantly reduced the incidence of AIRP (Ayat-Isfahani et al., 2017). Less arm and PIVC movements mean less friction of the catheter tip in the vein wall and less mechanical phlebitis.

2.4.5 Theme 5 Total dose

The total dose of amiodarone is an important predictor of phlebitis development. Norton et al. (2013) concluded that the total dose delivered via a peripheral catheter was the only significant predictor after analysing many factors predictive of phlebitis, and patients who had a total dose of 3 grams were found to be at a higher risk of phlebitis.

The duration of administration is also related to phlebitis development, but it is highly correlated with the total amiodarone dosage. An initial literature review indicated that differences in amiodarone infusion rate, total dose, duration, and concentration can affect phlebitis rate. This means that the longer the administration duration, the higher the total dose and the greater the risk of phlebitis (Oragano et al., 2019). Ward and Yalkowsky (1993) confirmed that precipitation worsens with prolonged and increased contact of amiodarone with the vein wall (as cited in Oragano et al., 2019). Oragano et al. (2019) found that total amiodarone doses greater than 1g had higher phlebitis rates than doses less than 0.45mg. They also found that the incidence of

phlebitis was lower with bolus administration than with more prolonged infusions. A total dose greater than 1 gram was consistently associated with increased phlebitis rates (Oragano et al., 2019). Overall, a higher dose of amiodarone is linked to an increased risk of phlebitis.

2.4.6 Theme 6 Distinguishing between intravenous catheter complications

Nurses often grapple with distinguishing among various intravenous (IV) complications. Notably, subtle differences exist among phlebitis, thrombophlebitis, extravasation, superficial skin cellulitis, and infection (Te Whatu Ora Canterbury, 2022), each presenting a distinct diagnosis that necessitates unique management strategies. Most PIVC phlebitis cases are unrelated to infection (Mermel, 2017). However, while typically non-serious, phlebitis requires supportive care and typically resolves within 1-2 weeks (Brors et al., 2023; National Health Service, 2022). In contrast, thrombophlebitis, associated with VIP stages 4 and 5, demands more attention. According to local organisational policy, a VIP score of 5, accompanied by oozing, purulent fluid, or exudates from the site, warrants a swab for culture, alongside laboratory analysis of the IV cannula tip, particularly when systemic infection is suspected, mandating prompt initiation of treatment (Te Whatu Ora Canterbury, 2022).

Extravasation signals a scenario where the PIVC are outside the vessel lumen, causing drug or fluid leakage into surrounding tissues (Te Whatu Ora Waitemata, 2023). Clinical manifestations include severe pain, burning or stinging sensations, oedematous changes resembling a raised area near the cannula site, alterations in skin colour involving blanching or redness, and the potential formation of blisters, with a progression toward ulceration (Te Whatu Ora Canterbury, 2022). Superficial skin

cellulitis, conversely, represents an inflammatory response within the tissue (Te Whatu Ora Waitemata, 2021). It occurs when bacteria infiltrate via the insertion site, traversing the extra luminal pathway of the cannula and the management approach centres on antibiotic treatment as prescribed by the doctors (Te Whatu Ora Canterbury, 2022).

Infection, a distinct concern, may arise from improper cannula insertion or substandard management and care, often traceable to non-compliance with aseptic technique principles (Helm et al., 2015; Higginson & Parry, 2011). Typically located at the catheter-skin entry point, infections may escalate to healthcare-associated bloodstream infections (HABSI), necessitating systemic antibiotics for resolution (Te Whatu Ora Canterbury, 2022). The clinical signs and symptoms of superficial skin cellulitis, phlebitis/thrombophlebitis and extravasation are similar, except there are small differences, which makes it difficult to differentiate these conditions. However, an infection has other severe presentations, e.g., purulent discharge or systemic symptoms, fever, tachycardia, and hypotension (Te Whatu Ora Canterbury, 2022).

In essence, differentiating between these PIVC complications is crucial for prompt and tailored interventions, enhancing patient outcomes and minimising potential risks. Although these complications can happen during infusion, there is also a risk of post-infusion phlebitis, which can occur after infusion and 24-96 hours post PIVC removal (Urbanetto et al., 2017). Such clinical acumen highlights the significance of nursing training in recognising, managing, and mitigating these diverse intravenous catheter challenges.

2.4.7 Theme 7 Phlebitis treatment

There are many options available for phlebitis treatment: pharmacological interventions, including anticoagulants, anti-inflammatories, and vasodilators; phytotherapeutic products using herbs and plants, including chamomilla recutita, notoginseny, and marigold/calendula ointment and physical measures using cold and heat (Hidayah et al., 2017; Jourabloo et al., 2017; Martin et al., 2017: Varghese& Kt, 2018).

Other therapeutic methods found in the literature included nitroglycerin in the form of transdermal patch and gel; creams containing heparin or polysulfate of mucopolysaccharide, also known as heparinoid substances (i.e., Hirudoid, Sankyo Pharma GmbH, Pfaffenhofen, Germany); notoginseny cream; and diclofenac in gel and oral form (Dos Reis et al., 2009). Despite many available treatments, there has yet to be an agreement about the optimal products (Garcia-Exposito et al., 2023).

Cold and heat

The application of alternating hot and cold compresses is proven effective in reducing erythema, oedema, and pain. The hot compress promotes vasodilation by improving blood circulation and accelerating wound healing. The cold compress stimulates vasoconstriction and decreases oedema (Annisa et al., 2017). Applying hot or cold compresses is believed to create a moist environment favourable for phlebitis reduction (Bryant & Nix, 2015, as cited in Annisa et al., 2017).

Systemic treatment

According to Di Nisio et al. (2015), systemic administration of pharmaceuticals is only occasionally used but mostly used when topical treatments are utilised. The Infusion

Nurse Society (2021) recommend providing analgesics or using pharmacological interventions such as administering anti-inflammatory agents, applying warm compresses and elevating the limb.

There are many available products, but some need to be approved for use in New Zealand. There is a need for more pertinent studies on treatments for infusion related phlebitis. Therefore, topical treatment for PIVC phlebitis needs to be further identified in the New Zealand hospital context. However, immediate catheter removal, topical application of anti-inflammatory agents, and hot and wet compress are effective treatments.

2.5 Summary

The international literature on Amiodarone infusion related phlebitis (AIRP) reveals a complex interplay of factors that can influence its genesis, including the use of an inline filter, amiodarone drug concentration, total infusion dose, IV cannula site, size and insertion technique, PIVC maintenance and care. The following methodology chapter will delve into the approach taken to investigate the factors that lead to amiodarone infused phlebitis in a local cardiac centre.

Chapter 3 Methodology

The study's overall purpose was to examine how and why amiodarone infusion related peripheral intravenous phlebitis (AIRP) occurred in the context of a local cardiac Centre. Yin's multiple case study method and design were followed. This chapter presents the research questions, rationale, and context of the case study, along with the philosophical underpinnings and the methods of data collection and analysis. The ethical considerations for the undertaking of the study are also outlined.

3.1 The context of the case

This study was based on an adult cardiac monitor centre consisting of a seven-bed coronary care unit and an 18-bed cardiology ward in a large metropolitan hospital in New Zealand. It primarily looks after patients needing services ranging from coronary or cardiac interventions, cardiac device implants, care of dysrhythmia, cardiomyopathy, acute coronary syndromes and other cardiac related symptoms or diagnoses. The researcher is a registered nurse working on the unit, and after noticing that many patients ended up with amiodarone induced phlebitis wanted to explore the phenomenon of how and why amiodarone induced phlebitis occurs and whether the service follows recommended local guidelines and whether these were in line with global guidelines. A case study methodology was chosen to triangulate a retrospective cohort of adult patients who received peripheral IV infusions of amiodarone during hospital admission and who developed amiodarone related phlebitis in the cardiac centre and compared these results to the processes outlined in local policy guidelines.

3.2 Research questions

Through the implementation of a mixed method "two multiple-case study "design, the following research questions guided this inquiry:

- How does the incidence of AIRP compare in the cardiac centre being examined to global incidence?
- Why are patients receiving AIRP at risk for phlebitis?
- How are AIRP treated in the cardiac centre?
- What and why are there gaps between local policies and best evidenced guidelines?

3.3 Rationale

The case study methodology is best suited to investigate a contemporary phenomenon within its real-world context when the boundary between phenomenon and context is unclear (Yin, 2018). The "case" in a case study can be referred to as the object of the study or the phenomenon being examined. Yin's method assumes that understanding the study object will likely involve important contextual conditions pertinent to the case (Yin, 2018). Originally, the interest in looking into the problem of AIRP came from multiple incident reports filed by nurses in the cardiac centre, which attracted the nurses' and their managers' attention. Reviewing current literature indicated various causes, including drug materials, patients, the health care facility (e.g., local policies) and personnel (e.g., nursing PIVC insertion and maintenance practice). A case study methodology was thought to capture these elements' influence for a more in-depth and holistic understanding of AIRP in the local context.

The case study approach is used as a mode of inquiry to reach research objectives. It answers how and why questions when the researcher has little or no control over variables and behavioural events (Yin, 2018). Case study research involves an in-depth examination of a specific system, referred to as a case, or several such systems, referred to as cases, over a certain period. This investigation thoroughly collects detailed data from various sources, e.g., observations, interviews, audio visual material, documents, and reports, and then reports a case description and case-based themes (Creswell et al., 2007). This methodology enables researchers to evaluate, explain, describe, illustrate, and enlighten complex phenomena. It deals with a technically unique situation where the number of variables of interest exceeds the available data points (Yin, 2018). It also allows researchers to capture different facets of the case using multiple data sources and triangulation. The case study method informs theory, practice, and decision-making (Yin, 2018).

Yin's case study approach involves concrete steps taken as a method of inquiry. Designing a case study starts with identifying the research problem-associated issues, defining the case, and refining the research questions (Schoch, 2020).

The development of propositions before beginning the data collection and analysis phase can guide the research with a clear framework and focus. A research proposition is a statement about an observable phenomenon that may be considered true or false (Merriam, 2009). Propositions can be generated from literature or an issue, serving as a purpose for the study (Yin, 2018). The research proposition in this study is that there are many amiodarone phlebitis events. It aims to gain insights from the inquiry for making practice change recommendations and improving quality of care because, in

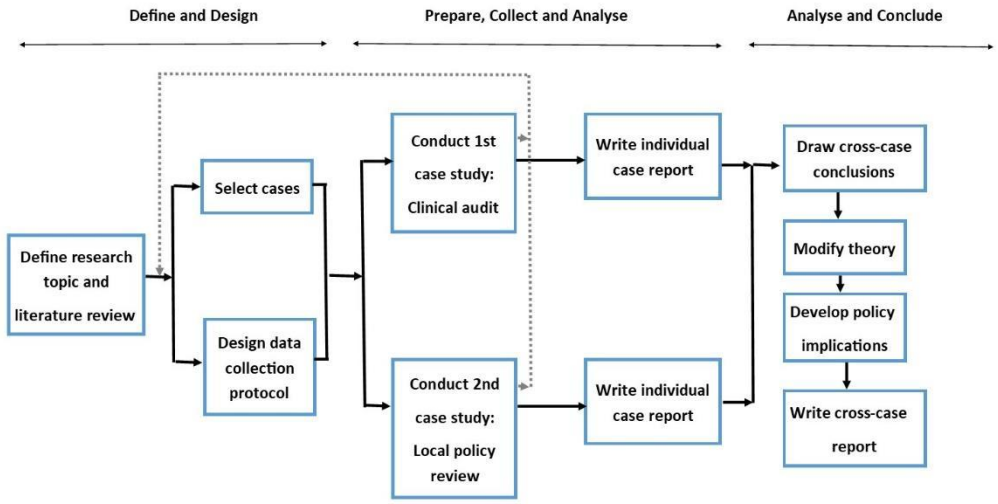
the literature, implementing evidence-based practice guidelines has been shown to reduce AIRP incidences (Mindo, 2018; Murphy et al., 2020; Spiering, 2014).

This case study chose multiple data sources to provide more perspectives to understand the phenomenon. This type of research is conducted when more than one case could provide much more depth or understanding of a topic (Yin, 2018). Within this research, individual cases are selected, believing that gaining insights from them will result in a deeper understanding and improved theory from a broader set of cases (Denzin & Lincoln, 2011). Using multiple case designs creates a more compelling story, thus making the research more robust (Herriott &Firestone, 1983). All these add to the benefit of using multiple cases.

This case study analysis used a cross-case synthesis approach. The design's purpose is to describe each case's uniqueness while allowing for the analysis of themes across multiple cases (Yin, 2018). Stake (2003) noted the value associated with analysing cases for comparison, which adds power to the study by allowing an examination of how the cases are similar and dissimilar (Yin, 2018). The primary objective of the analysis was to identify issues within each case and then purposefully explore the themes that commonly transcend the cases (Yin, 2018). The final analysis includes individual reports for each multiple-case study and a section to draw cross-case conclusions from the two multiple case studies and write a cross-case report. The analysis should delve deeply into the specific context in which the case presents itself (Creswell, 1998). Figure 3 is a flow chart illustrating these two multiple-case study research processes.

Figure 3

The research process using two case studies



Adapted from Yin (2018), p. 60

3.4 Philosophical underpinnings

This research used pragmatism as its philosophical underpinning to emphasise the practical implications of the findings in the clinical context. Pragmatism is a research paradigm in which the truth of an idea is determined by its practical results and how well it works in practice rather than relying solely on principles or ideology (Mayumi & Ota, 2023). It is an ongoing inquiry process to obtain the value of applying theories to find the answer to a specific question (Zambas et al., 2015). In nursing, pragmatism is essential for engaging in inquiry-based practice and translating knowledge into practice (Younas, 2020). Pragmatism focuses on problems with real-world impacts, such as phlebitis, which has been a long-existing complication of IV amiodarone

infusion. The philosophical underpinning fits well with Yin's definition of the case study as an in-depth investigation of a contemporary phenomenon in a real-world context with blurred boundaries (Yin, 2018).

Derived from the Greek word meaning "action", pragmatism focuses on consequences and meanings assigned to actions. Pragmatism deems action fundamental to knowledge, emphasising practical utility (Dolan et al., 2022). The core concepts of plurality, truth, fallibilism, subjectivity, and meliorism are highly applicable to nursing (James & Sheffield, 2019). Plurality refers to diversity and multiple approaches in a context, with truth emerging through experience. Truths are seen as provisional, gradually approaching absolute truth over time. Fallibilism acknowledges uncertain human knowledge, allowing for openness to corrections and critique. Subjectivity recognises personal influence on interpretations, lacking absolute objectivity. Meliorism believes in improving the world through human efforts and action, addressing challenges pragmatically (James & Sheffield, 2019).

In summary, pragmatism's focus on practicality and experiential truth-seeking aligns well with nursing principles and offers the following benefits in nursing research. Firstly, it reduces the practice research gap. At the same time, it can produce workable and context-specific knowledge and practice actions for nursing. Secondly, it provides meaningful data to support new truths. It can adopt multiple perspectives to inform nursing practice better. It also embraces the provisional nature of truth (Dolan et al., 2022). Pragmatism's practicality brings nursing research and practice close together.

3.5 Data Collection Methods

Case studies use “cases” as units of inquiry. The following pieces of data were collected to provide a detailed, rich and triangulated understanding of AIRP.

3.5.1 Case 1 -Artefact data/ archival records

A clinical audit examined 37 cases of AIRP occurring in the cardiac centre over seven years. An individual incidence of phlebitis is a primary unit of analysis. Thirty-seven individual cases were included in a multiple-case study to develop dominant themes about what contributed to the amiodarone phlebitis events.

The 37 cases were archival records of incident reports. The hospital Information Technology Department screened through the incident report data of all the inpatients who received IV amiodarone infusions and ended up with phlebitis during their hospital stay during a seven years between March 31, 2016, and June 12, 2023. Exclusion criteria included:

- AIRP occurring in other wards rather than the cardiac centre.
- Phlebitis related to other drug infusions.

Based on the literature review done earlier in this thesis, a data collection form was designed that detailed the common variables that contribute to the development of phlebitis during an amiodarone infusion (See Table 2). This form was used to audit the 37 cases to get the preliminary data extracted and ready for analysis.

Table 2.

Data collection tool for the audit data of AIRP in the cardiac centre

Case number	Age
Sex	Diagnosis
Date PIVC inserted	PIVC needle gauge
PIVC site	Grade of phlebitis as per VIP scale
Use of inline filters	Length of time infusion administered when phlebitis started (in hours)
Total amiodarone dose infused over a number of hours	Any treatment required (e.g., antibiotics)
More than 1 PIVC used during amiodarone infusion?	Dedicated PIVC for amiodarone infusion

3.5.2 Case 2 - Documents

The second case that was studied was a collection of local policies. Because documents exist independently of the research, they are a product of the context in which they were produced and grounded in the real world. They are “objective”, “nonreactive to the research process”, “unobtrusive”, and easily accessible pieces of data and can help

facilitate new understandings for the study (Merriam, 2009. p.155). A systematic search was conducted on the hospital Intranet, including controlled documents and on the web-based clinical decision support system. All the written documents related to phlebitis treatment in the organisation were reviewed. This process involved our steps: 1) finding relevant material; 2) once the documents were located, their authenticity was assessed; 3) Coding and cataloguing documents were done; and finally, content analysis was used to analyse the documents (Merriam, 2009). Four local policy documents from the organisation around amiodarone infusion and treatment of phlebitis make up the second multiple-case study (see Table 3).

Table 3

Local policies

No.	Local policies	Document source	Year
1	Amiodarone –Intermittent Infusion (Adults)	Local controlled documents	2020
2	Amiodarone-Continuous Infusion (Adults)	Local controlled documents	2020
3	Intravenous-Peripheral Cannulation & Care	Local controlled documents	2018
4	Skin and soft tissue infections-Adults	Local controlled documents	2021

3.6 Data Analysis

In a multiple-case study, the analysis has two phases: the within-case analysis and the cross-case analysis. During the within-case analysis, each case is initially considered as a comprehensive case in and of itself. The objective is to collect data that enables the

researcher to understand contextual variables that could influence the specific case as much as possible (Merriam, 2009).

Case one: To analyse 37 cases in the clinical audit, patterns, concepts, trends, and relationships within the data were sought. Two analytic techniques were used from Yin's method: explanation building and cross case synthesis. Explanation building involves understanding each case and detailing why things happen in the way they do. Cross case synthesis entails comparing and synthesising data across multiple cases to identify overarching themes, similarities, and differences that contribute to validating the propositions (Yin, 2018).

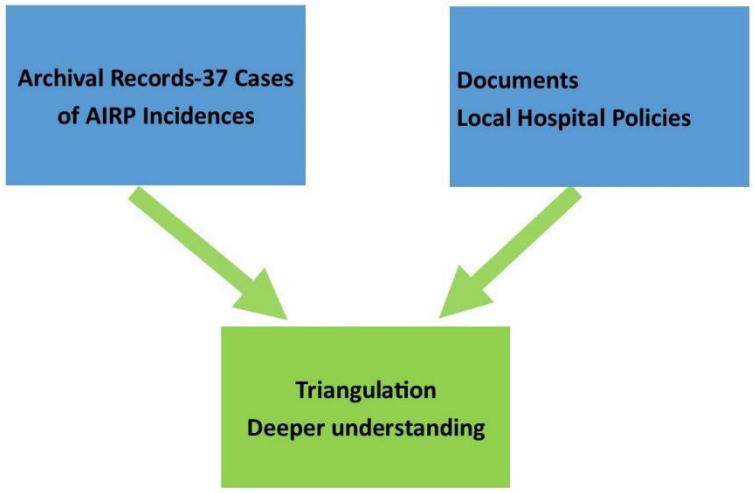
Case two analysis was the local policy review; the analysis process began by reviewing the collected documents. Documents were reviewed systematically to promote consistency of content and interpretation. The system began with those documents that were most closely related. After reviewing each document, notes detailing the elements most appropriate to the research questions were taken. As themes emerged, they were coded. The resulting group analyses were utilised to inform the coding and interpretation of the documents.

3.7 Triangulation

The final method used in this cross-case analysis was triangulation. Triangulation is where multiple data sources are utilised to find similarities and differences. Similarities increase the credibility of research findings (Cresswell, 2009). Triangulation increases transferability within and across each bounded case (Guba & Lincoln, 1994). This thesis triangulated the findings of archival records and documents (see Figure 4).

Figure 4

Process of triangulation



3.8 Researcher's background

The researcher is a registered nurse in the local cardiac centre, the study context. Because the researcher conducted the clinical audit and analysed the documents, it was acknowledged that this has the potential for assessment and reporting biases that might impact the study. To avoid bias, reflexivity was used, where the researcher was constantly aware of their feelings, opinions and prejudices and also used the supervisor to double-check for meaning and accuracy (Schoch, 2020).

3.9 Ethical consideration

Because patients were involved in this study, ethics was needed from the Auckland University of Technology Ethics Committee number 23/70 (see Appendix C). A locality

agreement was granted through the Research and Knowledge Centre from the organisation being studied (see Appendix D). A deidentified electronic data extract was obtained from the local hospital IT department. The data collection ensured patient confidentiality by gathering deidentified information without the patients' hospital identity numbers and other personal details. Every collection form used a unique identifier. All the information was transferred in a secure and passcode-protected manner. All data collected were stored electronically with passcodes that only the supervisor and primary researcher were in possession of. The data will be destroyed after six years.

3.10 Summary

This chapter has covered the methodology, theoretical underpinnings and methods used for this study. The next chapter will detail the audit findings and review local policies and documents.

Chapter 4 Results

This chapter presents the clinical audit findings of amiodarone infusion related phlebitis over seven years from March 31, 2016, to June 12, 2023, in the examined cardiac centre. It also presents the findings of the local policies and document analysis along with an overview of the triangulation of the two that summarises the important contributing factors of AIRP in the local context.

4.1 Case Study (clinical audit) results

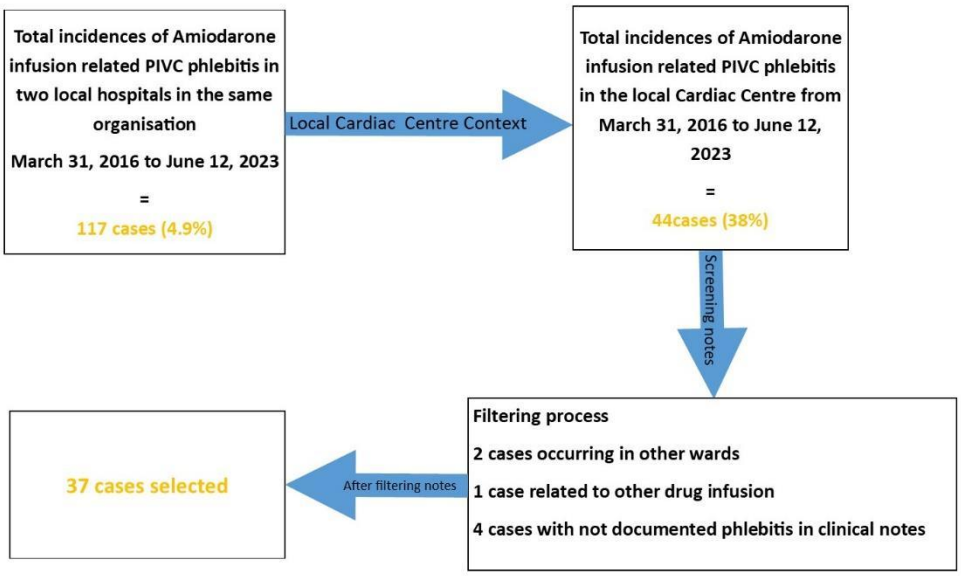
4.1.1 Description overview and statistics

The total number of patients who received an amiodarone infusion was 2388 over seven years from March 31, 2016, to June 12, 2023, across two hospitals (the cardiac unit in question and a sister hospital). There were 117 amiodarone infusion related phlebitis cases; therefore, the percentage of amiodarone infusion related phlebitis was 4.9%.

In context to the cardiac unit in question and without data from the sister hospital, a total of 443 patients (18.6%) out of a total of 2388 patients received amiodarone infusions. Of this, 44 of the 117 cases of amiodarone related phlebitis (38%) are represented by the cardiac centre in this period. This number was reduced to 37 cases as seven of the cases were excluded due to amiodarone related phlebitis occurring in other wards rather than the cardiac centre (2 cases), phlebitis related to another drug infusion (1 case), and there was no documented phlebitis in the clinical audit notes (4 cases). (See Figure 5). Therefore, the incidence of AIRP in the cardiac centre is 8.4% (37 cases out of 443 patients).

Figure 5

Thirty-seven cases selected from the clinical audit



4.1.2 Results of the audit

Patient demographics

The demographic information of the audit details (see Table 4, Figures 6 & 7). Most patients are 65 years and older (68%) and male (68%).

Table 4

Patient demographics

Age	**No. of patients**	**Percentage**
Under 65	12	32%
>=65	25	68%
Total	**37**	**100%**
Gender	**No. of patients**	**Percentage**
Male	25	68%
Female	12	32%
Total	**37**	**100%**

Figure 6

Age distribution of patients

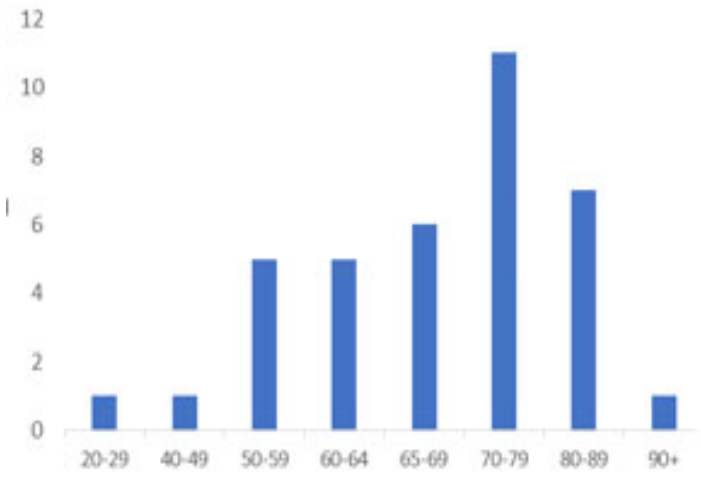
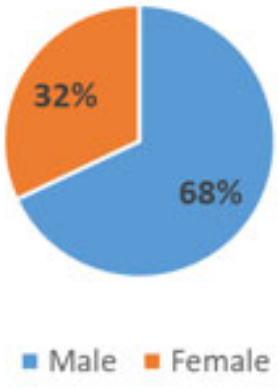


Figure 7

Gender distribution



Reasons for receiving amiodarone

Atrial fibrillation with rapid ventricular response was the most prominent reason patients received amiodarone. For statistical purposes, atrial flutter is classified into the same category, followed by Ventricular tachycardia (VT) and a combination of AF & VT or wide complex tachycardia (see Table 5).

Table 5

Diagnosis for IV amiodarone infusion

Diagnosis	**No. of patients**	**Percentage**
Atrial fibrillation (AF)/atrial flutter with rapid ventricular response	24	65%
Ventricular tachycardia (VT)	5	13%
VT/VF (ventricular fibrillation) arrest	3	8%
Combination of AF& VT or wide complex tachycardia	5	14%
Total	**37**	**100%**

Location of the intravenous site.

The location of the intravenous site was analysed, with most cases being in the Ante cubital fossa, followed by the forearm (see Table 6 and Figure 8).

Table 6

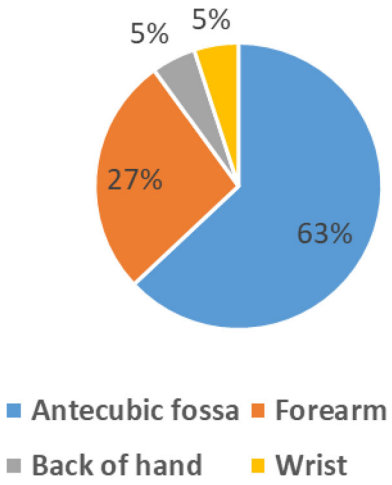
Location of IV amiodarone infusion related phlebitis

Total Number of PIVCs audited		40*	**Percentage 100%**
Location	Ante cubital fossa	25	63%
	Forearm	11	27%
	Back of hand	2	5%
	Wrist	2	5%

* A total of 40 PIVCs were audited as some patients had two PIVCs with phlebitis

Figure 8

PIVC location



Gauge and cannula

The following table and figures give a breakdown of the cannula gauge used across the 40 peripheral cannula sites. Only 30 PIVCs out of 40 audited PIVCs (75%) had confirmed gauges, with 25% having no clearly documented gauge. (See Table 7. The use of gauge 20 and bigger PIVCs was 90% (see Figure 9).

Table 7

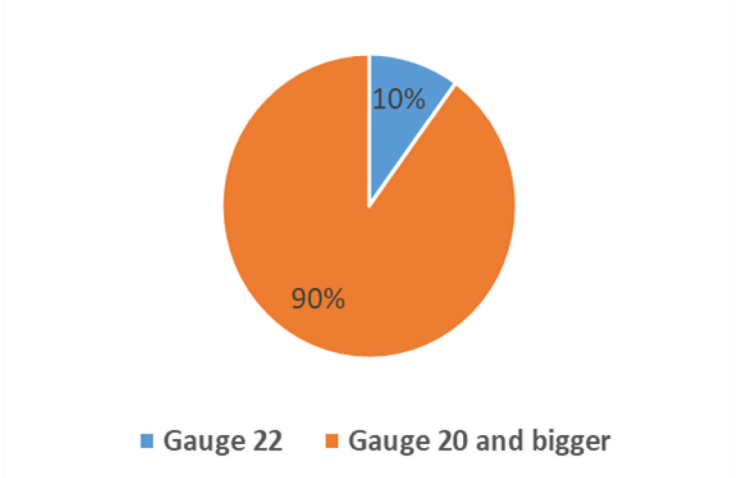
Sizes of PIVCs with IV amiodarone infusion-related phlebitis

Size	Number	Percentage
16g	1	
18g	13	
20g	13	
Unknown	10	
Total	**40**	**100%**
Gauge 22	3	10%
Gauge 20 and bigger	27	90%
Total	**30**	**100%**

Note: There is no entry on the electronic PIVC assessment form for PIVC located on the wrist, so nurses can only indicate the back of the hand or forearm.

Figure 9

PIVC size



VIP Scoring

The use of VIP scoring to assess the phlebitis severity was observed across the 37 patients. Before discovering the phlebitis, all the documented VIP scores were zero (39 out of 40 cannulation sites with phlebitis); only in one case VIP score was rated with a score of 1 out of a possible score of 5. After patients developed phlebitis, grading of phlebitis severity was not recorded using the VIP scales except in three cases (VIP scoring 2 in two cases and VIP scoring 3 in one case). Descriptive assessment information was used instead of using the VIP scoring and the words used to describe the sites include: “painful”, “red”, “bruised”, “inflamed”, “hard”, “firm”, “lumps”, “swollen”, “extending”, “spreading”, “blistery”, “pus looking centre”, “hot to touch”, “warm to touch “, “palpable cord”, “stinging”, “itchy”.

Infusion dose

According to the local organisation policy, an intermittent amiodarone infusion dose is usually 150mg over 30 minutes or 300mg over 60 minutes or may be given over 20 minutes and up to 2 hours. The continuous infusion dose is based on the patient’s weight. If less than 60kg, the policy states to give 600mg over 24 hours as a starting dose and titrate according to response; if the patient is more than or equal to 60kg, the policy states to give amiodarone 900mg over 24 hours. The infusion may be repeated at a maximum of 1200mg amiodarone in 24 hours unless under the cardiologist’s discretion. The protocol is generally followed hospital-wide.

The next result shows the infusion protocol. In this case study, 30 patients (81%) received an amiodarone infusion based on standard organisational protocol. Six

patients (16%) received amiodarone infusion with a special dosing regimen. One case has an unclear amiodarone dose (See Table 8).

Table 8

Amiodarone infusion dosing

	Cases	Percentage
Standard protocol		
A bolus dose of 300mg over 1 hour followed by 600mg/900mg over 24 hours	23	62%
600/900mg continuous dose without loading dose	5	13%
Two of 300mg loading dose followed by 600mg continuous dose	1	3%
One of 150mg loading dose followed by 900mg continuous dose	1	3%
Total	30/37	81%
Special dosing protocol		
Two of 150mg loading dose, then 300mg over 3-4hours followed by 900mg continuous dose	1	
Two of 150mg loading dose over 2 hours, 300mg over 3 hours, 600mg over 6 hours	1	
The slow infusion rate was to avoid hemodynamic disturbance, E.g., 200mg over 3 hours; once the initial intermittent infusion is complete, wait for 2 hours; if the patient remains in AF, then give another 300mg bolus and monitor.	1	
150mg over 1 hour, then 150mg over 1 hour, and another 150mg over 3 hours.	1	
300mg over 2 hours, 150mg over 1 hour	1	
The patient received multiple infusions due to reoccurring conscious ventricular tachycardia: on the first day, patient received 300mg bolus, then another 300mg over 1 hour; on the second day, patient received 150mg over 1 hour, 150mg over 2 hours, on the third and fourth day, patient received 900mg twice over 24hours	1	
Notes not available to do an analysis	1	
Total	7/37	19%

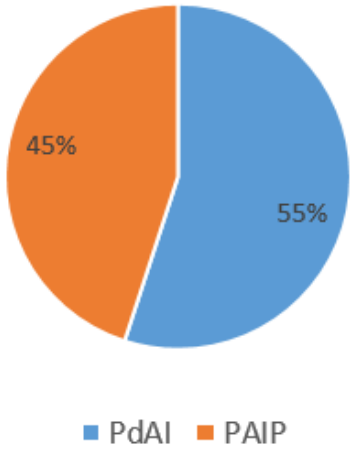
Timing of phlebitis during or after the infusion

Data on whether phlebitis occurred during or after the amiodarone infusion is shown in Figure 10. When phlebitis occurred during the amiodarone infusion, two or more

PIVCs were required to complete the infusion. To conclude, 45% of phlebitis cases occurred during the amiodarone infusion, and 55% occurred post amiodarone infusion.

Figure 10

Phlebitis during Amiodarone Infusion (PdAI) and Post Amiodarone infusion phlebitis (PAIP)



Treatment

The key themes among nursing interventions are warm compress in 3 cases (8.1%) and cold compression, including cold flannel or ice in 15 cases (40.5%). Other interventions noted were arm elevation, marking erythema and monitoring any extension; analgesia, e.g., Panadol if required.

Twenty-six out of 37 patients were seen by the medical team (70.3%). Twenty of 37 patients (54.1%) were charted oral antibiotics as treatment, with 4 cases (11%) requiring IV antibiotics.

4.1.3 Other findings

In one case, an ultrasound showed occlusive thrombosis of the basilica and ante cubital veins, diagnosed as a superficial vein thrombosis (SVT), this was even though the patient was receiving dabigatran (an oral anticoagulant). Doctors started the patient on prophylactic Clexane (low molecular weight heparin), then consulted the thrombosis team with the advice of giving Clexane for 2-3 weeks, then rescan. There was another case of possible thrombophlebitis, and doctors charted prophylactic Clexane.

There was no hold-up of discharge from the hospital due to IV amiodarone infusion-related phlebitis. Patients were discharged on oral antibiotics if needed. Education was given to self-medicate Clexane at home.

In one case, a patient had a central venous catheter (CVC) not used for amiodarone infusion.

In one case, there was a documented drug adverse reaction of amiodarone-related phlebitis on the patient's medication chart.

4.2 Document analysis

On analysis of the four local policy documents, a summary table was created to showcase what is recommended best practice for the facility and to note any overlap in the documents, if there were any (see Table 9). The documents included were: 1) Amiodarone -Intermittent Infusion (adults), 2) Amiodarone-Continuous Infusion (adults), 3) Intravenous-Peripheral Cannulation & Care, and 4) Skin and soft tissue infections-Adults. Local policy summary.

Table 9
Local policy summary

Amiodarone strength	Amiodarone hydrochloride 150 mg/3mL (1&2)
Infusion concentration	Intermittent infusion: 1mg/mL if 150mg over 30mins 1.2mg/mL if 300mg over 60 minutes (1) Continuous infusion: 1.8mg/mL if 900mg in 500mL D5 (dextrose 5%); 1.2mg/mL if 600mg in 500mL D5 (2)
Use a CVC	If infusion concentration exceeds 2mg/mL or repeated infusions are anticipated to avoid thrombophlebitis (1&2)
Inline filters	Not used (1&2)
Use amiodarone immediately after dilution	Yes (1&2)
Dedicated line	No (1&2)
Volumetric pump	Yes (1&2)
Low absorption bag	Yes (1&2)
Non-DEHP giving sets	Yes (1&2)
Flushing	20mL Normal Saline after each infusion (1&2)
Cannula site Inspection	Regularly for signs of extravasation (1&2)
Cannula size	Not specified for amiodarone infusion (1&2); choose the smallest and shortest length for the purpose (3).
Cannula location	If possible, avoid the ACF or any flexion area unless identified as needed for the procedure, treatment or emergency (3). Avoid areas of poor skin integrity (oedema, local infection, broken areas, bruising) (3).
Securement	Secure the extension with tape to prevent disruption (3)
Documentation	Each PIVC must have an insertion and maintenance record (3) document on insertion, and after that, once per shift, the VIP score is included in this documentation (3).
Cannula dwell time	72-96 hours (3)
Practice post Extravasation	Stop medicine/infusion, remove it, inform the medical team, and arrange a new IV site if required. Document in clinical notes (3).
Practice if infected (VIP score 2+)	Remove the cannula, swab the site if purulent fluid or exudate is evident and send for testing of M.C.S., (microbiology, culture and sensitivity). If systemic infection is suspected (line-related sepsis), the cannula tip should be sent for M.C.S, perform a septic screen and obtain two sets of blood cultures. Fill out an incident form and documentation in the patient's notes (3).
Empiric antibiotics treatment for superficial skin cellulitis	The first line for non-severe limb superficial skin cellulitis is flucloxacillin 500mg PO four times/day-1g PO three times/day unless penicillin allergy (4) Antibiotics prophylaxis is not appropriate for all patients and must always be discussed with ID (4).

4.3 Triangulation

The findings from case study one (the audit) and case study two (the policy review) are triangulated as outlined in the methods section of this thesis. This enables an overview of the similarities and differences and shows whether practice reality aligns with local practice standards (see Table 10).

Table 10

Triangulation of two cases with evidence based recommendations

	Local policy	Current practice aligns (Yes/No)
Amiodarone strength	Amiodarone hydrochloride 150 mg/3mL (1&2)	Yes
Infusion concentration	Intermittent infusion: 1mg/mL if 150mg over 30mins 1.2mg/mL if 300mg over 60 minutes (1)	Not always
	Continuous infusion: 1.8mg/mL if 900mg in 500mL D5 (dextrose 5%); 1.2mg/mL if 600mg in 500mL D5 (2)	Yes-81% of the time
Use a CVC	If infusion concentration exceeds 2mg/mL or repeated infusions are anticipated to avoid thrombophlebitis (1&2)	Yes- no patients received an infusion concentration greater than 2mg/mL
Inline filters	Not used (1&2)	Yes- No filters used
Use amiodarone immediately after dilution	Yes (1&2)	Not assessed
Dedicated line	No (1&2)	Unclear
Volumetric pump	Yes (1&2)	Yes
Low absorption bag	Yes (1&2)	Yes
Non-DEHP giving sets	Yes (1&2)	Yes
Flushing	20mL Normal Saline after each infusion (1&2)	Not assessed
Cannula site Inspection	Regularly for signs of extravasation (1&2)	Yes-every 8 or 12hourly
Cannula size	Not specified for amiodarone infusion (1&2); choose the smallest and shortest length for the purpose (3).	No-90% of cannula size gauge 20 and above

Cannula location	If possible, avoid the ACF or any flexion area unless identified as needed for the procedure, treatment or emergency (3). Avoid areas of poor skin integrity (oedema, local infection, broken areas, bruising) (3).	No-63% located at ACF
Securement	Secure the extension with tape to prevent disruption (3)	Not assessed
Documentation	Each PIVC must have an insertion and maintenance record (3) document on insertion, and after that, once per shift, the VIP score is included in this documentation (3).	Not always
Cannula dwell time	72-96 hours (3)	Not assessed
Practice post Extravasation	Stop medicine/infusion, remove it, inform the medical team, and arrange a new IV site if required. Document in clinical notes (3).	Yes

4.4 Summary

This study evaluated the contributing risk factors and treatment approaches for AIRP at a local cardiac unit. These results evaluated an audit finding (Case 1) and compared them to local guidelines (Case 2). These findings will be discussed in the next chapter with the addition of a comparison to global literature, along with recommendations that can be presented to the cardiac unit to improve practice. This chapter will also discuss the strengths and limitations and end with a conclusion.

Chapter 5 Discussion

This thesis aimed to gain insights into the causes of Amiodarone infusion related phlebitis (AIRP) in a cardiac centre. And was guided by four questions:

1. How does the incidence of AIRP compare in the cardiac centre being examined to global incidence?
2. Why are patients receiving amiodarone infusion via a peripheral intravenous catheter at risk for developing phlebitis?
3. How are AIRP treated in the cardiac centre?
4. What and why are there gaps between local policies and best evidenced guidelines?

The following discussion will answer these questions and discuss the findings in the chronological order presented in the results chapter.

5.1 Phlebitis rates

The phlebitis rate in the local cardiac centre was 8.4% over the last seven years, from March 2016 to June 12, 2023. This finding is low compared to the wide spectrum of phlebitis rates that ranged from anywhere between 0%-85% stated in the literature (Bagheri-Nesami et al., 2015; Boyce & Yee, 2012; Kochiadakis et al., 1999; Martinho & Rodrigues, 2008; Norton et al., 2013). Oragano et al. (2019) found that with 2114 patients, the overall phlebitis rate was 14%. However, the 8.4% found in this case study is a little above the acceptable benchmark rate of 5% set forth by the Infusion Nurse Society (2007, as cited in Oragano et al., 2019).

The substantial variation of reported phlebitis rates in the literature can be related to study designs, making an average benchmark difficult to obtain. For example, there are differences in the sample populations, practice standards of drug administration, and method of data collection across the studies (Ayat-Isfahani et al., 2017; Boyce & Yee, 2012; Norton et al., 2013). Norton et al. (2013) agree and suggest that different sample populations, dosages, routes of administration, and data collection methods were used in each study, making it difficult to ascertain the true phlebitis rate. Ayat-Isfahani et al. (2017) mentioned that the potential risk factors of amiodarone induced phlebitis include underlying pathological conditions such as diabetes mellitus, hypertension and higher rates were seen in those who are cigarette smokers, all of which may lead to heterogeneity. Other variances could be due to small sample sizes, which can skew the results (Oragano et al., 2019). Different sampling techniques introduced an element of selection, performance, and detection bias, which is likely to have played a role in the variability observed in phlebitis rates (Oragano et al., 2019). Overall, the incidence of ARIP in the cardiac unit could still be improved and reduced to a hospital-wide goal of zero.

5.2 Demographic findings

This case study found that most of the patients who experienced ARIP were 65 years and above (68%), and the same percentage identified as male (68%). Having a higher age presenting with AIRP is a significant demographic trend that aligns with several previous research findings (Boyce & Yee, 2012; Brors et al., 2023; Norton et al., 2013; Cheewatanakornkul et al., 2022; Spiering, 2014) (see Table 11). Martinho and Rodrigues (2008) found that age is an intrinsic cause of phlebitis, as older patients often have fragile veins, and the inner lining of their blood vessels is more susceptible

to inflammatory processes (as cited in Oragano et al., 2019). Older adults may also have weakness in peripheral vasculature due to comorbidities that impact vein health (Buzatto et al., 2016). Additionally, the reason why older adults are seen more frequently with phlebitis is that they are more predisposed to cardiac events that require medical intervention, such as amiodarone. Ageing leads to structural changes in the cardiocirculatory system, compromising electrical conduction and increasing cardiac arrhythmias, with AF being the most common condition in older patients requiring emergency care and IV amiodarone administration for reverting ventricular and atrial arrhythmias (Buzatto et al., 2016).

Another common theme across these studies is most of the patients are male (Boyce & Yee, 2012; Brors et al., 2023; Norton et al., 2013; Cheewatanakornkul et al., 2022; Spiering, 2014) (see Table 11). This is probably due to a higher male prevalence of atrial fibrillation in all age groups, with men also having an increased risk of sudden cardiac death (Westerman & Wenger, 2019; Wolbrette et al., 2002). Men with AF tend to have more coronary artery disease and develop postoperative AF at a higher rate than women (Westerman & Wenger, 2019). Female sex hormones are protective against atrial fibrillation, which may explain why the incidence of atrial fibrillation rises in post-menopausal women (Westerman & Wenger, 2019). The Cardiovascular Health Study, a substantial investigation involving 5201 older participants, revealed that cardiovascular events were 17.6 and 42.7 occurrences per 1000 person-years for men aged 65 to 74 and 75 to 84, respectively. In contrast, women in the same age categories experienced 10.1 and 21.6 events (Sankaranarayanan et al., 2013.). However, Buzatto et al.'s (2016) study found that among 102 patients older than 60,

17 out of 63 males (27%) and 17 out of 39 females (44%) developed AIRP, concluding that AIRP happened more frequently in women (43.6%).

Table 11

Patient demographics in other studies

Authors	Study period	Participants	Male	Age
Boyce & Yee (2012)	June to November 2009	12	83%	75% of patients>65
Brors et al. (2023)	March to May 2021	124	67%	The mean age was 70.6 years
Norton et al. (2013)	April 2018 to January 2019	105	71%	The mean age was 66 years
Cheewatanakornkul et al. (2022)	January 2017 to December 2019	214	61.7%	The mean age was 73 years
Spiering (2014)	March to June 2012	34	68%	The average age was 69

5.3 Medical conditions for receiving amiodarone

This case study found that atrial fibrillation (AF) or atrial flutter with rapid ventricular response was the most prominent reason patients received amiodarone, with 65% of the participants being diagnosed with this disorder in this case study. Similarly, in the literature, AF was most patients' main reason for treatment (Brors et al., 2023; Boyce and Yee, 2012; Cheewatanakornkul et al., 2022; Norton et al., 2013). Atrial fibrillation is a cardiac rhythm disorder characterised by rapid, disorganised excitation of the atria and irregular activation of the ventricles (Westerman & Wenger, 2019). As age is the

most significant risk factor for AF, the prevalence of AF shows a strong age dependence varying from 0.5% in patients aged <40 years to 5% in patients aged >65 years and nearly 10% amongst people of 80-89 years old (Sankaranarayanan et al., 2013). Buzatto et al. (2016) noted that AF is the most frequent condition in older adults admitted to emergency services.

5.4 PIVC location in antecubital fossa

In this case study, the incidence of AIRP was highest for infusion sites in the antecubital fossa (ACF). Peripheral cannulas placed in this region had a 63% prevalence of phlebitis, which raises significant concerns as it is often the vein of choice in peripheral vein selection. The local policy states to avoid this area if possible and recommends replacement in different locations (Te Whatu Ora Waitemata, 2023). The high rate of ACF cannulation remains a challenge not only in the local cardiac centre but also across many acute healthcare settings (Brors et al., 2023; Buzatto et al., 2016; Ruegg et al., 2021; Yasemin & Nuray, 2022). An Australian hospital survey done in 2018 revealed that 60% of all PIVCs were inserted in the ACF (Ruegg et al., 2021). Yasemin and Nuray (2022) found that 50% of phlebitis occurred more commonly attached to the ACF area. Brors et al. (2023) also found that most PIVCs were placed in the ACF (35%) among those who developed AIRP.

It is imperative to increase nursing awareness of avoiding ACF insertions. Nurses prefer ACF veins due to their larger size and better visibility for catheter insertion. Researchers conducted a survey in an Australian study aiming to reduce hospital-acquired bloodstream infections associated with peripheral IV catheters. They discovered that 24% of the respondents were unaware of the increased infection risk

with ACF (Ruegg et al., 2021). However, PIVC at ACF was still used regardless for amiodarone delivery. Murphy et al. (2020) created multidisciplinary guidelines based on the literature and conducted a quality improvement project to compare the incidences of AIRP during the pre and post intervention period. The study has shown better results for reducing AIRP by incorporating PIVC site selection criteria as part of the improvement process. Therefore, this is a potential place to start to reduce AIRP.

The recommended best nursing practice from the literature is selecting the most appropriate anatomical location based on the patients' condition, medication regimen, or treatment plan. Nurses must comprehensively assess the patients' vascular network and gather information about the patients' previous experiences before cannulation (Santos-Costa et al., 2022). Some international protocols advise against re-cannulation within the same vein below a recently utilised site to promote vein healing (National Health Service-Worcestershire, 2015). So, a bottom-up approach should be adopted to replace PIVC, or it is recommended to choose a different arm when phlebitis or other complications occur (Te Whatu Ora Canterbury, 2021). The recommended order of preference for peripheral infusion sites includes the forearm (basilica, cephalic and median antebrachial), the dorsum of the hand, and the wrist, followed by the antecubital fossa (Butler et al., 2021).

These practices must be explicitly outlined in the organisation's local policies for IV cannulation management or amiodarone infusions, and it is important to implement these. The overarching objective should focus on preserving the patients' blood vessels, preventing complications, and enhancing the patient experience over ease of access.

5.5 PIVC size

The local policy provides some guidelines for selecting PIVC size: the policy at the hospital states to choose the smallest and shortest length for the purpose; a 22-gauge catheter should be used for cytotoxic therapy and small, fragile veins. When looking at the demographic age who receive amiodarone, they are often older, have underlying cardiac conditions or have undergone cardiac surgery, and have more vulnerable and fragile veins (Gorski et al., 2015). This case study found that 68% of patients were 65 or older. Therefore, the integrity of their veins may be compromised.

When choosing PIVC size, best practice guidelines recommend inserting a small PIVC into a large vein with the rationalisation that a large PIVC inserted into a small vein can induce localised trauma (Higginson & Parry, 2011) and mitigate phlebitis rates (Spiering, 2014). The rationale as to why a small PIVC into a large vein is due to improved hemodilution of acidic drug solutions within larger veins (Yalkowsky et al., 1998 & Gorski et al., 2015). This practice is also advocated by the Infusion Nurses Society (2021), who rationalise that this practice enhances blood flow. Moreover, larger gauge catheters reduce the buffer space between the PIVC and vein wall, elevating the risk of mechanical phlebitis (Marsh, 2019). Thus, it is vital to adopt a cautious approach, adhering to the preferred 22-gauge size and utilising the forearm site, as clinical practice guidelines recommend (Spiering, 2014).

This case study found that IV amiodarone infusion-related phlebitis in the cardiac centre occurred with PIVC gauges 20 and larger (90% of the cases). Using a 20 gauge or larger catheter infers a lack of awareness at the local cardiac centre. This observation aligns with Brors et al.'s study, which identified phlebitis rates of 42% for medium

PIVCs (20-gauge) and 37% for large PIVCs (18-gauge), highlighting poor adherence to clinical practice guidelines regarding PIVC size (2023). Furthermore, only 5% received small-sized (22-gauge) PIVCs at the recommended forearm location.

In practice, nurses often opt for larger PIVCs, particularly for cardiac procedures involving IV contrast, emergencies, or large fluid boluses (Ruegg et al., 2022). However, local policies must stipulate smaller PIVCs specifically for amiodarone infusion, reflecting a gap in awareness and specificity for this drug.

5.6 Use of VIP score to assess phlebitis severity

Within the cardiac centre, nursing staff routinely employ the VIP score for IV cannula assessment. However, a notable need for more consistency exists in employing the VIP scale to assess the severity of existing phlebitis for diagnostic and interventional guidance. Particularly, when patients developed phlebitis, the grading of this complication using the VIP scales was infrequently documented, with only three cases displaying VIP scores (two cases with VIP score=2 and one with VIP score=3). Rather, nursing notes provided descriptive assessments, encompassing terms such as "painful," "red/bruised," "inflamed," "hard", “firm," "lumps," "swollen," "extending," "spreading," "blistery," "pus-looking centre," "hot/warm to touch," "palpable cord," "stinging," and "itchy." This lack of documentation potentially resulted in underreporting phlebitis incidents, as some PIVCs were removed without documented reasons, and a site assessment was rarely charted in correlation with the PIVC removal.

Although the VIP assessment tool is recommended as a guide for measuring phlebitis, nurses need to focus on other important factors. It was argued that the current VIP

assessment tool predominantly focuses on measuring phlebitis while overlooking other prevalent PIVC complications, including occlusion, infiltration, extravasation, dislodgement, and infection (Ray-Barruel & Rickard, 2017). This argument raises pertinent questions about the comprehensiveness of the VIP score in the local organisation with only three documented scores above O. It prompts considerations for developing more inclusive tools to capture the full spectrum of PIVC related complications. While the VIP score offers a structured approach to assess phlebitis severity, its effectiveness may be limited when addressing the multifaceted challenges arising from PIVC failures. Consequently, incorporating more comprehensive assessment strategies into the organisational policy might enhance the overall evaluation of PIVC related complications and improve patient care.

5.7 Infusion dosing

In this case study, 30 patients (81%) received an amiodarone infusion based on standard organisational protocol. Six patients (16%) received an amiodarone infusion with a special dosing regimen. Of these 16%, 5 out of 6 received special dosing regimens consisting of intermittent bolus infusions, which are not in the scope of the local policy. Local policy states that 150-300mg doses may be repeated to a maximum of 1200mg amiodarone in 24 hours. If the dose exceeds 1200mg in 24 hours, the decision should be discussed with a cardiologist. The usual dose of 150-300mg dose may be given over 20 minutes to 2 hours (Te Whatu Ora Waitemata, 2020). Whether the intention of slowing the infusion rate was to avoid hemodynamic disturbance, these special regimes tend to infuse amiodarone in small doses over longer periods with some pauses in between. Amiodarone administered as a bolus has shown lower phlebitis rates than in studies in which amiodarone was administered as a continuous

infusion (Norton et al., 2013; Oragano et al., 2019). Although continuous infusion is more prone to AIPR, it is accepted practice to deliver amiodarone continuously- this can, however, be a risk factor that can be flagged to staff to consider being more vigilant around.

Concentration is also a variable that needs to be taken into consideration. According to Cheewatanakornkul et al. (2022), an amiodarone concentration of 1.5mg/mL is safe and can prevent phlebitis. In the local policy, the intermittent bolus dose concentration is 1mg/mL for 150mg and 1.2mg/mL for 300mg, and this is what the audit found being done in practice in the cardiac centre. Therefore, supposedly, intermittent amiodarone infusions should be safe. However, infusion duration can be a contributing factor, and Buzatto et al. (2016) found that the absence of phlebitis only happened in exclusive bolus infusions of a maximum of 30 minutes.

5.8 Post amiodarone infusion phlebitis

This case study found that in the local cardiac centre, (55.3%) of the phlebitis incidents occurred during the infusion and (44.7%) occurred post-infusion. Brors et al. (2023) similarly uncovered a comparable pattern with (53%) of the patients in their study experiencing amiodarone induced phlebitis during infusion and (47%) post-infusion. Brors et al. (2023) study was one of the first to shed light that a substantial proportion of patients developing amiodarone-induced phlebitis get this in the post-infusion phase, thereby revealing an understudied component of this phenomenon. This knowledge gap necessitates vigilant monitoring of PIVC sites after amiodarone infusions, as these complications can appear 24-96 hours post IV amiodarone treatment. The local organisational policy aligns with these concerns and advises

discharged patients to consult a general practitioner should their infusion site show signs of swelling, redness, pain, or increased warmth upon discharge (Te Whatu Ora Waitemata, 2023). Consequently, these findings stress the importance of prioritising preventive measures for amiodarone-induced phlebitis throughout the entire intravenous treatment continuum, including the often-overlooked post-infusion phase.

5.9 Amiodraone infusion related phlebitis treatment

5.9.1 Use of antibiotics for treatment or prophylaxis

This case study found that 70% of the patients were reviewed by doctors when AIRP occurred. Then, among the 26 cases, doctors reviewed, 77% of the patients were given IV or oral antibiotics as treatment. The diagnosis given was either extravasation or superficial skin cellulitis. Local guidelines remind clinicians to be vigilant if there is a VIP>2 and assess for infection that may need treatment. Oragano et al. (2019) stated that a vein with untreated phlebitis can become infected and progress to infective phlebitis. The primary objective of the local policy revolves around maintaining a high level of alertness to prevent phlebitis from progressing to a more severe infective stage. This stance inevitably promotes the wide use of prophylactic antibiotics as a preventative measure.

However, antibiotic prophylaxis is not always appropriate for all patients, and improper use can lead to antibiotic resistance. The pervasive use of antibiotics may cause the spread of antibiotics' tolerance and resistance (Fymat, 2017). Besides, other complications, for example, allergic reactions of varying severity, diarrhoea related to C. difficile, and antimicrobial use can also lead to the selection of antibiotic resistant flora (Clark et al., 2019). It is hard to criticise the prevalent use of antibiotics in

practice, whether for prophylaxis or treating superficial skin cellulitis, as cellulitis mimics thrombophlebitis (Te Whatu Ora Waitemata, 2021). No guideline or recommendation for using antibiotics for PIVC extravasation exists. Recommendation of a standardised conservative treatment approach would minimise potential over-treatment with antibiotics, reduce costs and reduce anti-microbial resistance. This approach would benefit from future studies for validation. Whether antibiotics are necessary for most AIRPs should be challenged.

5.9.2 Cold compress vs. warm compress

This case study found that nurses in the local cardiac centre used cold compression in 40.5% of the cases as a management tool for ARIP; this included using a cold flannel or ice. The local policy states to use ice for extravasation. Divergent viewpoints within the literature mark the choice between cold and warm compresses. The goal is to decrease phlebitis's discomfort and speed up the healing process within a moist environment at the inflammation area (Annisa et al., 2017). Much effort has been made, such as applying warm or cold compresses to the site of phlebitis. While a warm compress could comfort the painful areas, inducing improved blood circulation and promoting a faster wound-healing process, a cold compress could stimulate vasoconstriction, reducing oedema (Bryant & Nix, 2015; Gauttam & Vati, 2016). However, applying alternating hot and cold compresses to reduce erythema, oedema, and pain is an evidence-based approach to address phlebitis related symptoms (Garcia-Exposito et al., 2023). It could be suggested as an option for the unit.

5.10 PIVC cannulation assessment

The current practice on the cardiac unit is to assess IV cannulas every shift; however, there is fluctuation in how often this would be as a typical shift may be either 8 or 12 hours, so there could be a difference that ranges from two checks in a 24hour (12-hour shift) to three checks (in a 24hour period if doing 8-hour checks). Both time allocations may fall short in early recognition and prevention of amiodarone infusion-related phlebitis. While the local amiodarone infusion policy mandates regular inspection of the cannula site for signs of extravasation, it lacks specificity regarding assessment frequency (Te Whatu Ora Waitemata, 2020). The literature offers varying recommendations, advocating for assessments and documentation occurring between 1 to 4 hours during the infusion and 4-hour intervals post-infusion and IV catheter removal (Cottrill, 2022; Murphy et al., 2020; Norton et al., 2013; Woods et al., 2022).

One post-intervention survey revealed that nurses strongly agree that regular documentation of phlebitis assessments significantly enhances patient care (Cottrill, 2022). This approach aligns with the proactive monitoring concept, aiming to address issues promptly. However, it is essential to note the potential resource and time constraints such a frequent assessment schedule may pose, particularly in busy clinical settings. A more tailored approach could be implemented, allowing flexibility based on individual patient factors, infusion duration, and local policies (Infusion Nurses Society, 2021).

Some evidence and this case study found that amiodarone-induced phlebitis can manifest 24 to 96 hours after infusion completion (Brors et al., 2023; Macklin, 2003). The local organisational policy advises patients to seek medical attention if specific

symptoms arise. The post-infusion phase remains understudied, prompting critical questions about the appropriate timing and frequency of assessments during this period. Currently, the hospital where this study was done uses an electronic health record system with a mandatory assessment box where peripheral intravenous catheters need to be checked every 8 hours using the VIP scale. There is a pressing need for further investigation and consensus-building within the cardiac centre being examined to establish evidence-based protocols for optimal patient care, both during and after amiodarone infusion, with an increased assessment time and more education given to staff.

5.11 Inline filter

This case study identified that no inline filters were used at all in the cardiac centre being studied and was not a requirement in the local guidelines; however, incorporating inline filters in amiodarone infusions has been widely advocated in some literature and various guidelines, yet its implementation is notably absent within the organisation. A Thai study did a retrospective propensity score-matched analysis to explore whether an inline filter would decrease the AIRP incidence in the high-concentration of amiodarone infusion compared to low concentration without an inline filter. It concluded that amiodarone infusions with concentrations lower than 1.5mg/mL yield only a minimal incidence of low-grade phlebitis, suggesting infusion safety without an inline filter (Cheewatanakornkul et al., 2022). Furthermore, another study has proposed that bolus infusions, particularly those with durations under 10 minutes, can be administered safely without an inline filter. Consequently, the local organisational policy aligns with these findings, deeming intermittent infusions safe without needing an inline filter. Since an inline filter is not implemented in the local

organisation, the benefits of incorporating an inline filter into 900mg continuous infusions as a precautionary measure are still to be uncovered.

Seeney's implementation of IV giving sets with filters for amiodarone infusion in Wellington, New Zealand (NZ) yielded a 30% reduction in PIVC phlebitis rates among cardiology and post-cardiac surgery patients (Sweeny, 2019). Using a 0.22µm filter may help reducing AIRP because, in the local policy, the continuous infusion has an amiodarone concentration of 1.8mg/mL, which is higher than the safe concentration of 1.5mg/mL but falls below 2mg/mL; the concentration threshold requiring a central venous catheter. Some other major hospitals in the metropolitan city where this case study was conducted use inline filters for amiodarone infusions. Medsafe is the regulatory body for medicines in New Zealand, aiming to maintain a favourable balance between advantages and potential risks associated with therapeutic products in the intended treatment population. Medsafe datasheets specified using inline filters for amiodarone infusions. What is concerning is that before changing to Te Whatu Ora-Health NZ (the national agency to replace the country's 20 District Health Boards), the old District Health Boards (DHB) did not appear to employ filters in a similar capacity. With Te Whatu Or-Health NZ now operating as a unified entity, there is a compelling case for integrating resources and policies among all hospitals. Standardising the national policy on inline filter usage, supported by evidence demonstrating its effectiveness, would significantly improve patient care and safety.

5.12 Using dedicated IV cannulas for Amiodarone infusion

This study did not specifically evaluate whether healthcare workers should use a dedicated IV cannula for amiodarone infusion. The utilisation of a dedicated peripheral

intravenous cannulas (PIVC) for amiodarone infusion emerges as a crucial yet variable practice among nurses within the examined setting from the writer's observations. The local policy neither mandates nor emphasises the need for dedicated PIVCs for amiodarone infusions, thereby resulting in diverse nursing practices, ranging from the continued use of the same line beyond 48 hours post-insertion to the concurrent administration of other medications through the same IV line during amiodarone infusion as witnessed during the auditing process. It is essential to highlight that policies strictly prohibit mixing amiodarone with other medications, including New Zealand Medsafe (2023) guidelines.

This practice variability reflects a need for more awareness among nurses regarding the importance of treating amiodarone infusion with specialised care. This may lead to the practice of using the same PIVC for other high-risk phlebitis-inducing medications, including specific intravenous antibiotics (IVAB), hypertonic infusions, blood transfusions, and hyperosmolar drugs (Johnson et al., 2023). It must be acknowledged that PIVCs are more likely to cause phlebitis during amiodarone infusions. Therefore, nurses need to use dedicated PIVCs to mitigate the risk of phlebitis.

In essence, the absence of a standardised approach in the organisational policy demands more guidance and education to increase awareness among nursing staff. These would not only ensure the dedicated use of PIVCs for amiodarone infusion but also promote patient safety and the prevention of phlebitis associated with it.

5.13 Implications for nursing practice

Based on the findings from this case study, there is a need to promote nurses' awareness of AIRP prevention and management.

Nurses must be vigilant about the high risk of AIRP when giving amiodarone infusion and adhere to evidenced best practices. Based on the results of this case study, the following protocol was designed by the author, called the ABCDEF protocol for amiodarone infusions. This protocol follows mnemonic alphabetical grouping or prompts that can be effective for training nurses and easily integrated into patient care protocols.

Table 12

The ABCDEF protocol for amiodarone infusions

A for Assessment	Assessment frequency: 1-4hourly during and post infusion/PIVC removal, using VIP score
B for Bigger veins	Bigger vein, better blood flow
C for Cannula	Smaller cannula size for maximal stability and minimal vein contact. Prioritise the use of IV placing a non-jointed area
D for dilution, documentation & dedicated line	Dilute in the compatible fluid to lower the concentration Proper documentation: VIP score each shift, hospital incident report Use of dedicated line. No other preparations should be injected into the same PVIC.
E for entanglement	IV site securement during infusion
F for filter and flushing technique	The advantage of introducing an inline filter is to be further determined. However, its utilisation can potentially add more benefits for reducing AIRP. Flushing with 20mL normal saline ensures the dose enters the central circulation and reduces the risk of local reactions at the injection site.

F stands for follow-up care after phlebitis	If infectious phlebitis is suspected, monitor for signs of systemic infection and call for medical review. If non-infectious, alternatively apply a warm and cold compress, provide analgesics as needed, and consider other topical pharmacological interventions. Antibiotics should be the last resort to prevent over prescription.

Z Song, (2023).

Incorporating a new protocol with the recommendations from this research requires an interdisciplinary approach involving various healthcare professionals to enhance patient outcomes associated with amiodarone infusion-related phlebitis (AIRP). Pharmacists may explore the implementation of in-line filters for amiodarone infusions within the organisation and assess the potential benefits of reducing amiodarone infusion concentrations. The medical team may consider the timely transition from intravenous to oral amiodarone and the prescription of topical treatments for phlebitis. Furthermore, there is an opportunity to establish the role of a vascular access nurse specialist, working with the anaesthetic technician team, to promote the utilisation of ultrasound guided peripheral IV cannulations for patients with challenging intravenous access within the hospital, and monitoring intravenous access complications. This initiative aims to improve the overall hospital experience and reduce the incidence of phlebitis during prolonged amiodarone infusions, offering an alternative through long IV lines or midlines.

Nurses must educate patients about the risks associated with amiodarone infusions and the signs and symptoms of phlebitis. In NZ, there is a transformational change to

the national health system, and one of the priorities is to improve equity and outcomes. As our healthcare system transitions to a value-based system, patient engagement and understanding of patient perspective are becoming increasingly important in assessing healthcare quality. Nurses need to look at patients as partners with the understanding that their input is important to their health journey. Informing and partnering with patients about the need for amiodarone infusion and encouraging them to play an active role by being alert to signs and symptoms of PIVC complications whenever possible enhances patient empowerment and improves outcomes.

5.14 Strengths and Limitations

This research has increased knowledge about amiodarone infusion related phlebitis in the cardiac centre. This study is the first to delve into this practice issue in this organisation. It is highly relevant because it can help provide excellent patient care by preventing amiodarone induced phlebitis. This can be achieved through research, nurse education and research translation into practice, aligning with the organisation's goals and values. Local policies should be updated to reflect best evidenced guidelines based on these findings.

There is limited existing research on Amiodarone infusion related phlebitis, and there are scarce articles with small datasets. These contribute to the challenge of generalisability. The incoherent study designs, such as differences in the sample populations, practice standards of drug administration, and data collection method across the studies, means that the study results are highly specific to the study context.

This case study is based on a single healthcare-centre. Though data collection covers seven years, the sample size is small; therefore, the results may be inaccurate. There may be underreporting of phlebitis cases, contributing to the low rate seen in this study. Another limitation could be that cases may have been missed because of the study's retrospective nature; sample selection is based on the result of the IT department searching clinical records using clinical codes "amiodarone infusion" and "phlebitis". Another limitation that could lead to underreporting of ARIP is that nurses are usually the first clinicians to report IV cannula complications. If signs and symptoms of phlebitis were noted but not interpreted as "phlebitis" or not documented in clinical records, it would not appear in the database.

The retrievability of the documentation was further complicated. During the seven years the retrospective data were collected, the organisation experienced digital transformation. It went from paper documentation for reporting amiodarone phlebitis to electronic data collection in 2019. It is noticeable that electronic records provide better data quality. For example, every IV cannulation assessment asks for all the relevant information before processing to submission. It is easier to audit electronic records than paper records, as there are more detailed and accurate information on PIVC insertion and maintenance form. Data collection from paper records appeared harder and more likely to be incomplete.

This case study is a single-person project for a master's dissertation done by someone who works in this cardiac centre. Therefore, there may be some reporting bias or inaccuracy. Although the supervisor was able to double check the data and findings. Another threat was the possibility of incorrect data entry or misinterpretation of data.

This research was conducted in its unique context as being a single cardiac unit in a large metropolitan city; therefore, it is generalisable to New Zealand and may limit generalisability to other countries. Ethnicity was not collected, which is also a limitation of this study. Risk factors were identified and based on a tool designed by the researcher based on a systematic literature review; therefore, only a selection of risk factors in the audit collection tool was focused on. Other important variables can lead to phlebitis, including body mass index, vein quality, nutrition status, presence of comorbidities, and psychological conditions, such as agitation. Besides, there are many other issues in practice, such as the venepuncture procedure that could have affected the results, including the skills of the PIVC inserter, the antiseptic method, the frequency of insertion trials, the use of ultrasound, and the use of gloves.

5.15 Recommendations for future research

It would be recommended to use the ABCDEF tool and do a pre-test and post-test to see if the rates of amiodarone infusion phlebitis improve after education. Further research is needed to see if prophylactic antibiotics are needed for treating phlebitis, when and how to use them. More research is also needed on the necessity of the use of inline filters.

For future research, it is advisable during the design stage to set up a “collecting information as you go” method with a logbook over some time, for example, six months, when the researchers can record needed information about each incidence of AIRP so that the data will be complete and more accurate. Then, the researcher could gather more data regarding the length of infusion administered when phlebitis started,

the percentage of applying various nursing interventions and the percentage of cases in which nurses did not use a dedicated IV line for amiodarone infusions.

Future studies could also expand on broadening the care contexts and sample size to improve generalisability. This project can spread from the cardiac setting to other contexts around the hospital and potentially improve the quality and consistency of care patients receive throughout the entire hospital. The study could also be adjusted to incorporate other medication infusions with a high risk of causing phlebitis, such as chemotherapy, antibiotics, and IV fluid infusion.

5.16 Conclusion

Amiodarone is an important antiarrhythmic drug commonly used in cardiac centres for treating supraventricular and ventricular arrhythmias. It is often administered via a peripheral intravenous line; however, its chemical makeup often causes phlebitis at the administration site. This research found that some gaps in current practice did not align with local policy or international best practices. These include the prominent use of the antecubital fossa as the site for IV administration and that a 20-gauge catheter or larger was predominantly used in place of the recommended 22-gauge cannula stipulated in the literature. Other areas for improvement include increasing PIVC assessment frequency, using VIP scores to assess phlebitis severity, monitoring for post infusion phlebitis, alternating warm and cold compresses for best treatment results, and arranging timely medical reviews along with using dedicated IV cannulas for amiodarone infusions along with consideration of inline filter for continuous amiodarone infusions. Now, there is a unified Te Whatu Ora Health NZ; steps should be taken to close the gaps. Therefore, better quality of care and patient outcomes can

be achieved by tackling these risk factors, implementing practice change and incorporating best practice protocols such as the ABCDEF- amiodarone protocol for amiodarone infusion administration could help decrease the rates of amiodarone infusion phlebitis.

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Appendices

Appendix A: Selected Articles

No.	Author/Year/Country	Purpose, e.g. Empirical study, conceptual analysis, policy	Key themes
1	Ayat-Isfahani, et al., 2017, Iran	Effects of injection-site splinting on the incidence of phlebitis in patients taking peripherally infused amiodarone: A randomized clinical trial	Injection site splinting
2	Bagheri-Nesami, et al., 2015, Iran	An Iranian double blind randomized controlled trial. Applying sesame oil topically to the infusion site of amiodarone is recommended to reduce the development rate of amiodarone-related phlebitis.	Sesame oil
3	Boyce & Yee, 2012, the USA	A study was done in six months to collect data: among 12 patients, various grades of phlebitis developed in 8 patients (67%). Phlebitis developed at 12 of the 24 infusion sites (50%).	AIRP incidences: percentage and severity
4	Brors et al., 2023, Norway	A prospective observational study with the aim to determine the incidence of IV amiodarone-induced phlebitis, to describe adherence to a clinical practice	AIRP incidences, nursing practice guideline adherence,

		guideline, and to determine how characteristics were distributed between those with and without phlebitis.	characteristics of phlebitis or without phlebitis
5	Buzatto, et al., 2016, Brazil	A prospective and observational cohort study to verify the incidence of phlebitis and identify factors associated with the development of phlebitis due to peripheral IV infusion of amiodarone in elderly patients.	AIRP contributing factors, elderly patients
6	Cheewatanakornkul, et al., 2022, Thailand	A retrospective propensity score-matched analysis to find out whether an inline filter will reduce the incidence of AIP in the high-concentration of amiodarone infusion compared to low concentration without inline filter	Inline filter
7	Hannibal, 2016, the USA	A review of AIRP and best practices to prevent AIRP using a case report.	AIRP, best-evidenced practices
8	Mory & Hartman, 2011, USA	A retrospective chart review and observational, before and after study to determine if peripheral IV amiodarone and vancomycin influenced the incidence of thrombophlebitis in an adult cardiothoracic population.	Infusion concentration related to AIRP
9	Murphy et al., 2020, USA	This evidence-based quality improvement initiative aimed to decrease and enhance early detection of phlebitis in patients receiving amiodarone.	Evidence based practice guidelines reducing AIRP incidences

10	Norton, et al., 2013, USA	This research reviewed clinical records of adult patients in an 18-month period who received IV amiodarone while in the critical care unit to determine the incidence and factors contributing to the development of AIRP to refine the current practice protocol.	AIRP incidence, drug dose, practice protocol
11	Oragano, Patton & Moore, 2019	A systematic review of studies in which amiodarone-induced phlebitis was a primary or secondary outcome.	AIRP contributing factors: inline filters, nursing guidelines, higher dose and concentration needs more surveillance
12	Sharifi-Ardani et al., 2017, Iran	A randomized, double-blind clinical trial, to assess if topical chamomile may be effective in decreasing incidence of phlebitis due to an amiodarone infusion.	Topical chamomile reducing AIRP
13	Slim et al, 2007, USA	The study examined the incidence of phlebitis in a postoperative patient population given current practice guidelines for peripheral IV administration of <2mg/mL.	AIRP incidence at guideline dose recommendations, in-line filer

14	Spiering, 2014, USA	A study compared the pre-guideline phlebitis rate to the post-guideline rate and suggested the implementing a peripheral amiodarone infusion guideline reduced the incidence and severity of AIRP in the cardiac population.	Peripheral amiodarone infusion guideline
15	Tinoco, et al., 2014, Brazil	This integrative review aimed at identifying scientific publications on AIRP and proposes a nursing care algorithm for interventions in IV amiodarone administration.	Nursing care algorithm/guideline/best practices
16	Woods, et al., 2022, the USA	A 4-phase study to identify a more suitable peripheral IV catheter for reducing AIRP. A collaborative effort between beside nurses and the vascular access team evolved to look at alternative products for peripheral IV catheters.	Practice change-implementing extended dwell PIVC.
17	Mindo, E., 2018, USA	This is a thesis for the Master of Science in Nursing. In a project, practice change was introduced. AIRP incidences were compared pre and post change.	Staff education, implementing evidence-based practice guidelines
18	Cottrill, K. , 2022, Australia	This is a dissertation for Doctor of Nursing Practice. This quality improvement project aimed to implement an evidence-based amiodarone infusion guideline to	Implementing nurse practice guideline

	reduce phlebitis development or severity in cardiac-surgery step-down patients without a CVC who received a peripheral IV amiodarone infusion.

Appendix B: Policy

New Zealand policies		
Amiodarone infusion policy	Wanganui Hospital	https://www.wdhb.org.nz/assets/Uploads/Documents/b9438c576b/amiodarone.pdf
Intravenous Amiodarone New Zealand Datasheet	Medsafe New Zealand	https://www.medsafe.govt.nz/profs/datasheet/l/Lodiinf.pdf
Notes on Injectable Drugs-Amiodarone hydrochloride		Book from New Zealand Pharmacist's Association
MIMS Book-Amiodarone		Book
Australian Hospital policies		
Amiodarone (Cordarone X) Intravenous administration	The Royal Hospital for Women	https://www.seslhd.health.nsw.gov.au/sites/default/files/documents/amiodarone2018.pdf
Drug guideline-amiodarone(Intravenous)	Grampians Health Ballarat	https://www.bhs.org.au/bhsapps/govdoc/gdhtmL/gddrg0023--25690-amiodarone%20july%2022%202021%20final.pdf
Hospital policies in England		
Amiodarone loading dose regimen	NHS-Gloucestershire Hospital	Amiodarone_yMQ78Us.pdf (gloshospitals.nhs.uk)

Prescribing information for the administration of amiodarone in adult patients	Maidstone and Tunbridge Wells NHS Trust	DRAFT ACCEPTANCE LETTER – F (mtw.nhs.uk)
Policies/guidelines in the USA		
Amiodarone	Authors: Jeffrey B; Alex Lucas; Daniel Girzadas	https://www.ncbi.nlm.nih.gov/books/NBK482154/#:~:text=To%20treat%20all%20acute%20tachyarrhythmias,should%20not%20exceed%202.4%20grams.
Amiodarone: Guidelines for Use and monitoring	Siddoway, L. (2003). American family physician, 68(11):2189-2197	https://www.aafp.org/pubs/afp/issues/2003/1201/p2189.html

Appendix C: AUTEC (Auckland University of Technology Ethics Committee) approval

4 May 2023

Rebecca Mowat
Faculty of Health and Environmental Sciences

Dear Rebecca

Re Ethics Application: **23/70 A multiple case study examining the risk factors contributing to intravenous amiodarone infusion related phlebitis: a nursing knowledge focus**

Thank you for your responses to AUTEC's conditions.

Your ethics application has been approved for three years until 4 May 2026.

Standard Conditions of Approval

1. The research is to be undertaken in accordance with the Auckland University of Technology Code of Conduct for Research and as approved by AUTEC.
2. All public facing documents must have the AUTEC approval number and be of a high standard of spelling and grammar. Dates on the Information Sheet(s) and Consent Form(s) must be consistent.
3. Any amendments to the project must be approved by AUTEC prior to being implemented.
4. A progress report is due annually on the anniversary of the approval date.
5. A final report is due at the expiration of the approval period, or, upon completion of project.
6. Any serious or adverse events must be reported to AUTEC, this includes unforeseen issues that might affect continued ethical acceptability of the project.
7. AUTEC grants ethical approval only. You are responsible for obtaining management permission for access from any institution or organisation at which your research is being conducted and you need to meet all ethical, legal, public health, and locality obligations or requirements for the jurisdictions in which the research is being undertaken.

The application number and title need to be referenced on all correspondence related to this project.

All forms are available online http://www.aut.ac.nz/research/researchethics

For any enquiries, please contact ethics@aut.ac.nz
(This is a computer-generated letter for which no signature is required)

The AUTEC Secretariat
Auckland University of Technology Ethics Committee

Cc: Zoe.Song@Waitematadhb.govt.nz

Appendix D: Locality Approval from Te Whatu Ora-Waitemata

发件人: Research & Knowledge Centre <research@waitematadhb.govt.nz>
发送时间: 星期二, 五月 9, 2023 2:13 下午
收件人: Zoe Song (WDHB) <Zoe.Song@waitematadhb.govt.nz>
主题: RM15489 - A multiple case study examining the risk factors contributing to intravenous amiodarone infusion related phlebitis: a nursing knowledge focus - Locality Authorisation

Dear Zoe,

The Research & Knowledge Centre has now received the relevant approvals for the following study:

Title: A multiple case study examining the risk factors contributing to intravenous amiodarone infusion related phlebitis: a nursing knowledge focus

Registration #: RM15489

This study now has Waitematā Locality Authorisation. Please continue to forward to us copies of all correspondence regarding ongoing ethics approval for this study (if any). All amendments to your study must be submitted to the Research & Knowledge Centre for review. Any substantial amendment (as defined in the Standard Operating Procedures for HDECs) must also be submitted to your ethics committee for approval.

Note that all research, audit and related activity must meet ethical standards in relation to the safe storage, retention and disposal of research data.

If you require a data extract from the information analysts, please email your requirements to HealthAnalyticsTeam@waitematadhb.govt.nz to be put in touch with the appropriate analyst. Discuss possible lead times given there is significant clinical demand on their services.

If you require access to any paper clinical records, once you have your list of patient NHIs please forward a copy of this email to Vanessa McGill (Vanessa.Mcgill@waitematadhb.govt.nz) with the NHIs requiring record retrieval. Describe what access you require and discuss possible lead times given there is significant clinical demand on their services.

At the conclusion of this study a copy of any outputs, reports or publications should be forwarded to research@waitematadhb.govt.nz

Good luck with your study.

Regards
Research & Knowledge Centre
Te Whatu Ora - Waitematā