Amiodarone is an antiarrhythmic drug indicated in the treatment of ventricular arrhythmias. Early studies evaluating amiodarone for the management of ventricular arrhythmias demonstrated the efficacy of amiodarone in patients who were refractory to treatment with multiple antiarrhythmic drugs. More recently, 2 major trials, published in 1999 and 2002, described the efficacy of amiodarone as a primary treatment modality in the treatment of ventricular arrhythmias compared with another antiarrhythmic drug, lidocaine, and placebo. As a result of this literature, the American Heart Association Advanced Cardiac Life Support (ACLS) guidelines recommend amiodarone as the antiarrhythmic of choice in the resuscitation of patients with ventricular arrhythmias.

The use of amiodarone for the emergent treatment of ventricular arrhythmias, including ventricular tachycardia and ventricular fibrillation, has steadily increased in recent years. This increased use is a result of emerging literature relating to the efficacy of amiodarone, combined with the updated ACLS treatment guidelines available from the American Heart Association. In the setting of cardiac emergency (eg, ventricular tachycardia with a palpable pulse), the recommended dose of intravenous amiodarone is 150 mg. In cardiac arrest (eg, ventricular fibrillation), the recommended dose of amiodarone is 300 mg administered intravenously, followed by a subsequent dose of 150 mg as needed for sustained arrhythmia. In the 2005 American Heart Association guidelines, the recommendation for administration of amiodarone is as an intravenous bolus dose. In the typical medical setting, the preferred standard of practice is to prepare an infusion of amiodarone diluted in 5% dextrose in water placed in a polyolefin bag, administered through an in-line filter via a central vein or large peripheral vein. However, in the setting of cardiac emergency, administration by prolonged infusion is not desirable. The vast differences in the recommendations for administration of amiodarone in this setting have raised significant questions in the medical community.

Amiodarone: A Complex Antiarrhythmic Drug

Amiodarone is a Vaughn Williams class III antiarrhythmic drug. It has a complex mechanism of action, with mechanistic properties that include action at α- and β-adrenergic receptors, as well as action on the potassium, sodium, and calcium channels in the heart. In general, the beneficial effects of amiodarone are due to its ability to prolong the cardiac action potential and refractory period. The efficacy of amiodarone in the treatment of ventricular arrhythmias is thought to be due to suppression of premature ventricular depolarization and the occurrence of further arrhythmias.

Amiodarone: Administration and Adverse Events

In the clinical trials that have evaluated the use of amiodarone for the treatment of ventricular arrhythmias, there has been a wide range of variability in the dose, rate of administration, and dilution of amiodarone. The range of amiodarone doses reported has ranged from 18.75 mg to 600 mg. Similarly, the rate of administration has varied widely, from rapid intravenous administration to infusion of up to 30 minutes. Based on all of the available literature to date, only 3 studies have reported rapid intravenous infusion of amiodarone. Each of these 3 protocols varied in the dilution of amiodarone, ranging from undiluted solution to dilution in either 20 or 30 mL of 5% dextrose in water.

Concerns have been raised regarding the rapid administration of intravenous amiodarone. This concern results from reports of numerous adverse events associated with the administration of amiodarone, the most notable of these adverse events being hypotension, bradycardia, and phlebitis.
clinical studies reported to date, the incidence of these adverse events has been highly variable, with the incidence of hypotension ranging from 7% to 59%, bradycardia ranging from 0% to 41%, and phlebitis ranging from 0% to 27%.1-15,18,19 However, an in-depth evaluation of the clinical studies that have evaluated the use of amiodarone for the treatment of ventricular arrhythmias reveals that the incidence of adverse events from administration of amiodarone appears to be relatively varied, regardless of the rate of administration or dilution of the drug.1-15,18,19

It is difficult to define the occurrence of adverse drug events in resuscitation trials and even more difficult to determine an association of adverse events with a specific drug therapy. For example, several clinical studies resorted to the definition of hypotension in the clinical trial as the need for vasopressor therapy (eg, dopamine) after the resuscitation.1-14 This definition is tenuous, because vasopressor supportive therapy of blood pressure is commonly required in post-cardiac arrest victims.15 The protective effect of simultaneous administration of potent vasoconstrictive drugs commonly used during resuscitation, such as epinephrine or dopamine, against the development of hypotension and bradycardia in this setting has been debated.3,15,18 Therefore, it would be difficult to deduce whether the hypotension, bradycardia, or proarrrhythmia observed in the clinical trials of amiodarone during cardiac arrest are in fact due to the primary cause of the arrest (eg, myocardial infarction), the loss of cardiac output during the arrest, or as the result of an adverse effect from amiodarone therapy.

Recommendations for Amiodarone Administration

Based on the results of recent research, amiodarone is the intravenous antiarrhythmic drug of choice for the resuscitation of patients with ventricular arrhythmias.16 Amiodarone is commercially available as a 150-mg, 3-mL vial.17 In the urgent treatment setting (eg, ventricular tachycardia with palpable pulses), a loading dose of amiodarone, 150 mg, is preferably administered in 100 mL of 5% dextrose in water over 10 minutes, as per the manufacturer’s recommendations.17 In the setting of cardiac arrest, some references have recommended rapid administration of undiluted amiodarone, followed immediately by a 10-mL flush with either 5% dextrose in water or 0.9% normal saline solution.18,20 Anecdotally, one practical method for rapid administration of amiodarone during cardiac arrest (eg, ventricular fibrillation) is to withdraw the contents of one 150-mg vial into each of two 10-mL syringes filled with 0.9% sodium chloride. These 2 syringes, for a total of 300 mg, could be administered via rapid intravenous infusion in the setting of cardiac emergency. Amiodarone should preferably be administered in a central vein; if central venous access is not available, administration should occur through the largest vein possible.

Summary

Recent literature has found amiodarone to be the antiarrhythmic of choice in the resuscitation of cardiac emergencies due to ventricular arrhythmias. As a result, the use of intravenous amiodarone has steadily increased. However, amiodarone has been associated with multiple adverse events, raising concerns regarding the appropriate administration of amiodarone in this setting. When administering intravenous amiodarone, the need for rapid administration, the risk for adverse events, and the clinical condition of the patient must be considered. In the case of life-threatening ventricular arrhythmias, rapid achievement of therapeutic drug concentrations and the suppression of further arrhythmia is a high priority. Therefore, in the setting of cardiac emergency (eg, hemodynamic instability with a palpable pulse), a recommended dose of intravenous amiodarone, 150 mg administered over 10 minutes with continuous cardiac monitoring, is appropriate. In the setting of cardiac arrest (eg, ventricular fibrillation), rapid intravenous administration of amiodarone, 300 mg, is reasonable. This method of administration can be accomplished in 1 of 2 ways: either via direct injection of the undiluted drug, followed by a minimum of 10-mL flush, or by minimally diluting each of two 150-mg doses within two 10-mL 0.9% sodium chloride–filled syringes.

REFERENCES


