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EM - REVIEW

Challenging the superiority of amiodarone for rate control in Wolff-Parkinson-White and atrial fibrillation

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Abstract The objective of this review is to explore and challenge the superiority of amiodarone for rate control in Wolff-Parkinson-White syndrome and concomitant atrial fibrillation (WPW-AF). The current recommendation for pharmacological treatment of this condition is amiodarone. A review of the past 25 years of literature finds several studies that identify a small risk of ventricular fibrillation secondary to amiodarone administration for rate control in WPW-AF. Additionally, the literature supports the safe and effective use of procainamide for rate control in WPW-AF. This review concludes that amiodarone is not superior to procainamide in rate control for WPW-AF, and may be dangerous.

Keywords Amiodarone · Procainamide · Wolff-Parkinson-White (WPW) · Atrial fibrillation

Introduction

We present a case of a patient with Wolff-Parkinson-White (WPW) syndrome and concomitant atrial fibrillation (AF) to demonstrate and discuss the controversy surrounding its treatment. The current recommendation for pharmacological treatment is amiodarone. In this article, we challenge its efficacy, as well as discuss the evidence behind procainamide use (Table 1).

Case presentation

A 39-year-old man presented to the Emergency Department (ED), complaining of 8 h palpitation and fluttering discomfort in his chest. The patient had a history of intermittent palpitations, but stated that he typically could meditate to help alleviate these symptoms. He reported that the palpitations typically occurred at times of stress or exertion. Approximately 3 years prior, he had been diagnosed with Wolff-Parkinson-White syndrome. Cardiac and stress testing were conducted without any further abnormalities or need for angiography.

The patient presented with the following vital signs: blood pressure 92/37 mmHg, pulse 209 beats/min (bpm), respiratory rate 24 breaths/min, and pulse oximeter 100%, although it is unclear if the patient was on supplemental oxygen. The patient was neither on any medications, nor had any follow-up since the WPW diagnosis. He stated that he had been doing well, with the exception of the intermittent bouts of palpitations. He denied dizziness, lightheadedness, or pain. The family history was non-contributory. He smoked cigars but denied cigarettes. The patient used marijuana, but denied cocaine.

He was alert and oriented and the skin was warm and dry. There was no jugular venous distension. He was tachycardic, but there was no wheezing, rales or increased work of breathing, and he denied shortness of breath and cough.

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Table 1 Antiarrhythmic comparisons for conversion to sinus rhythm in Wolff-Parkinson-White with atrial fibrillation (WPW-AF)

Study	Drug name	Dosage	Rhythm at presentation	Success in conversion to sinus rhythm
Boriani et al. [2]	Amiodarone	5 mg/kg in 20 min	AF, 250 bpm ventricular rate	Within minutes of the amiodarone bolus, patient converted into ventricular fibrillation. Cardioversion shock with 200 J resulted in successful conversion to normal sinus rhythm
Kappenberger et al. [5]	Amiodarone	600–800 mg/day	Induced AF	In 8/12 patients, the ventricular rate remained rapid after amiodarone infusion; these patients eventually underwent surgical ablation
Schützenberger et al. [13]	Amiodarone	5 mg/kg in 10 min	AF, 140 bpm ventricular rate with wide QRS complexes	Within 10 min of amiodarone administration, the ventricular rate increased to 210 bpm and the systolic blood pressure dropped to 80 mmHg. This condition persisted for 10 min before conversion to normal sinus rhythm was achieved
Sheinman et al. [15]	Amiodarone	1,200 mg in 24 h	AF, 130–170 bpm ventricular rate with narrow and broad complex tachycardia	Administration of amiodarone led to an increase in the ventricular rate, up to 230 bpm. 20 h post-admission, 150 mg disopyramide was administered. There was a sudden conversion to narrow-complex AF. 15 min post-disopyramide infusion, normal sinus rhythm was achieved
Fengler et al. [4]	Procainamide	Not mentioned in article	AF, rapid ventricular rate	Originally, the patient was treated with intravenous metoprolol 5 mg, leading to an increase in heart rate to 300 bpm. Intravenous procainamide was initiated, achieving conversion to normal sinus rhythm
Li et al. [6]	Procainamide	Unknown	AF	After intravenous procainamide infusion, conversion to normal sinus rhythm was achieved in 51 patients
Madrid et al. [7]	Sotalol	1.5 mg/kg in 10 min	Induced AF	After sotalol administration in 18 WPW patients with inducible AF, 4/18 converted to normal sinus rhythm during the infusion, 7/18 converted to normal sinus rhythm within 30 min of the infusion, and 7/18 remained in AF

AF atrial fibrillation

The rhythm strip demonstrated a wide-complex ventricular response between 200 and 220 bpm, occasionally dropping to 180–190 (Fig. 1) Given the known WPW syndrome, this was interpreted as AF. The systolic blood pressure intermittently dipped to 60–80 mmHg, despite IV fluids. The chest X-ray study was normal. Although 150 mg of IV amiodarone was administered, he remained tachycardic, at 200–210 bpm. The blood pressure continued to be labile, with a systolic blood pressure of 60–110 mmHg.

The patient was not initially cardioverted, as he had been symptomatic for 8 h, and tolerated the moderate hemodynamic compromise. Procainamide, though effective to simultaneously block the AV node and accessory pathway, was not chosen due to its more potent negative inotropic effect relative to amiodarone. The SBP, though stable, hovered in the low 1990s. Procainamide was not immediately available in the ED within 15 min, and the patient's blood pressure was low; had this not been the case, it could have been used instead.

Lidocaine has little to no negative inotropy, but is contraindicated in AF with WPW, as it slows AV conduction, but can facilitate antegrade conduction along the accessory pathway [11], resulting in increased rate, hypotension, or ventricular fibrillation [10]. Furthermore, the use of two sequential antidysrhythmic agents in the same patient is not recommended; synchronized cardioversion is the preferred treatment. The cardiology consultant also recommended amiodarone over procainamide through phone consultation.

Given lack of improvement with antidysrhythmic therapy, we began synchronized cardioversion (all with a

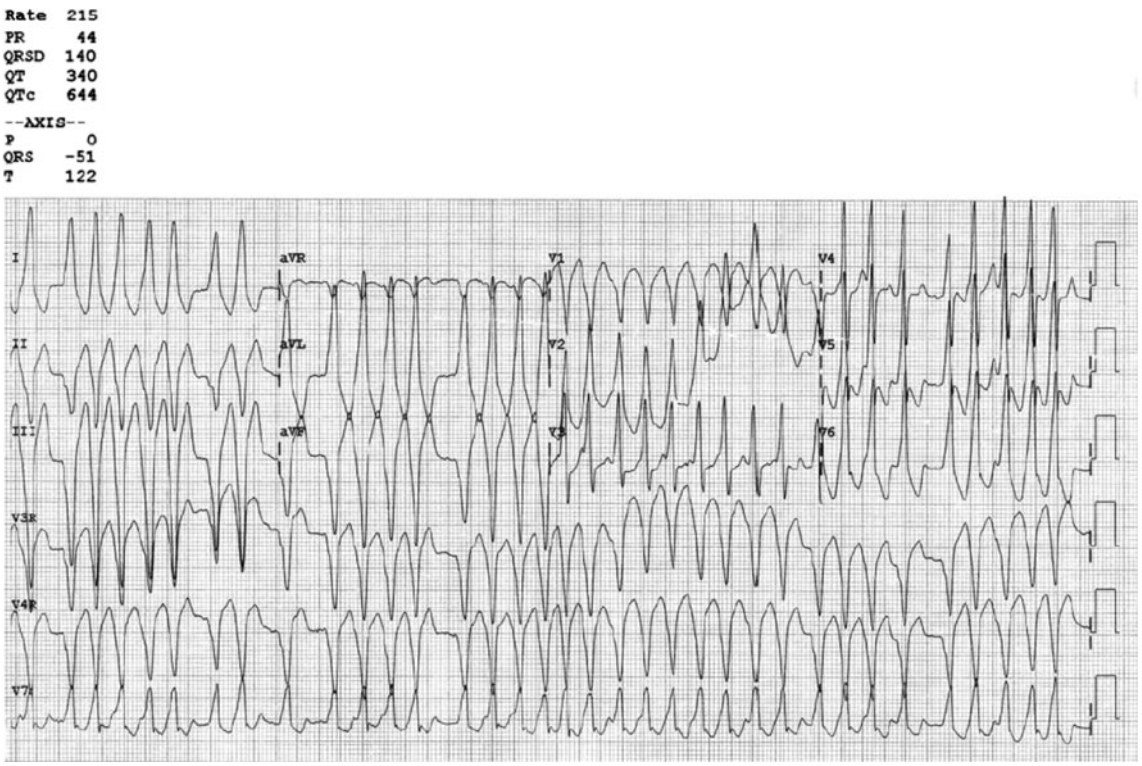

Fig. 1 Initial 15-lead EKG of our patient with wide-complex tachycardia, heart rate recorded at 215 bpm, and an irregular rhythm in leads V3R, V4R, and V7

monophasic defibrillator) approximately 30 min after the IV amiodarone administration. He received etomidate for sedation, was cardioverted with 70 J, and immediately developed ventricular fibrillation, losing consciousness. The patient was bag-valve-mask ventilated, intubated, and cardiopulmonary resuscitation was begun. He then received a 200 J defibrillation without resolution. We administered 1 mg of IV epinephrine (1:10,000) and defibrillated a second time at 300 J. He reverted to a wide-complex tachycardia at 140–160 bpm. The troponin level returned elevated at 0.22 μg/l (reference rate 0.00–0.09 μg/l), and he was started on heparin.

Initial pertinent laboratory values were normal magnesium 2.0 mg/dl (reference range 1.3–2.7 mg/dl), myoglobin 59 ng/ml (reference range 0–110 ng/ml), sodium 136 mmol/l (reference range 135–147 mmol/l), potassium 3.8 mmol/l (reference range 3.5–5.5 mmol/l), chloride 103 mmol/l (reference range 99–109 mmol/l), bicarbonate 25 mmol/l (reference range 20–31 mmol/l), calcium 9.3 mg/dl (reference range 8.7–10.4 mg/dl), and mildly elevated bun/creatinine ratio of 22/1.41 mg/dl (reference range 6–20/0.70–1.30 mg/dl). No further troponin or cardiac enzyme levels were recorded during this episode. As per the admitting cardiologist's recommendations, a 17 mg/kg loading dose of IV procainamide was given at 30 mg/min, followed by a drip at 2 mg/min. He converted to a normal sinus rhythm, rate 76 with Q-waves in the inferior leads of unclear chronicity, and no acute ST-T wave changes (Fig. 2). Repeat electrocardiogram displayed a sinus bradycardia, rate 54 bpm with inferior Q-waves, intraventricular conduction delay, and non-specific ST-T wave changes (Fig. 3). As the AF episode concluded, the vital signs were recorded at: blood pressure 84/55 mmHg, pulse 67 bpm and respirations 14 breaths/min. An echocardiogram showed normal left ventricular chamber size, wall thickness and motion, with an ejection fraction of 50%. Mild left atrial enlargement, normal mitral and aortic valves, normal right heart, and mild tricuspid regurgitation were also recorded. The patient was admitted to the hospital, and subsequently underwent electrophysiology study, ablation of an accessory pathway (AP) without complications, and cardiac catheterization revealing no significant coronary disease. The patient recovered and was discharged on hospital day 6.

Discussion

The American Heart Association (AHA) 2005 Cardiopulmonary Resuscitation Guidelines tachycardia algorithm solely recommends amiodarone for termination of ventricular tachycardia due to WPW-AF [1]. In this case

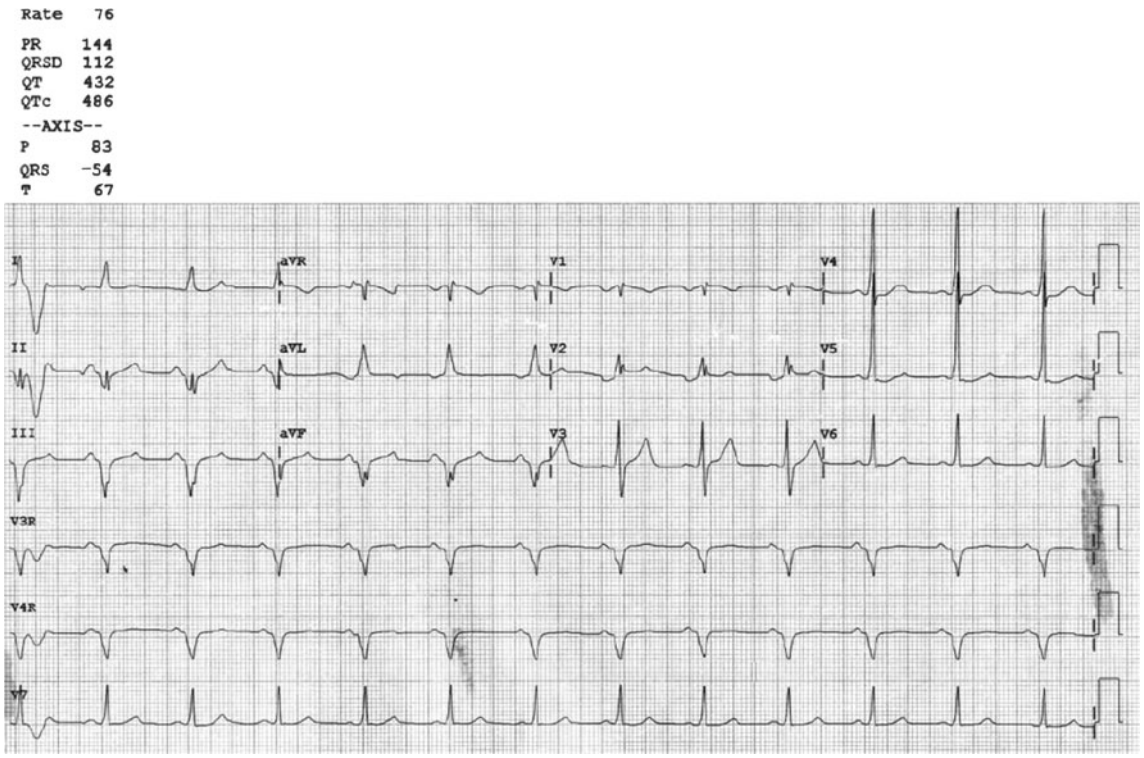

Fig. 2 15-lead EKG following ACLS and defibrillation for ventricular fibrillation with conversion back to normal sinus rhythm. Notice prominent Q-waves in inferior leads (II, III, AVF), but no ST-elevation or signs of acute myocardial infarction

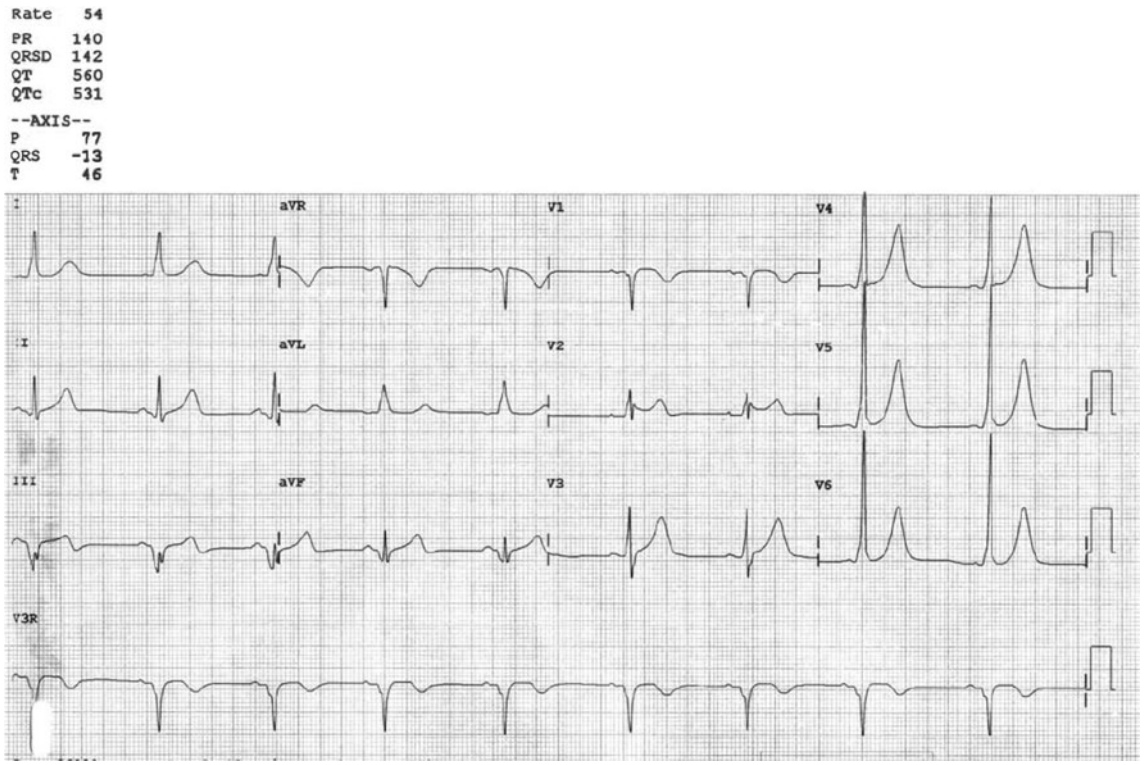

Fig. 3 12-lead EKG following monitoring and stabilization in the hospital, prior to discharge demonstrating continued Q-waves in the inferior leads (II, III, AVF), slight intraventricular conduction delay, and no further signs of ischemia or cardiac damage

report, we explore and challenge the basis for the superiority of amiodarone in the AHA recommendations.

Recent studies support the small yet serious risk of ventricular fibrillation secondary to amiodarone administration for rate control in WPW-AF. The 1996 Boriani case report concludes that amiodarone may lead to prodysrhythmic events in WPW-AF. The case report recommends the use of class 1A or 1C antidysrhythmic drugs in place of amiodarone in WPW-AF [2]. Similarly, in 2005, Tijunelis and Herbert published a review article on amiodarone in WPW-AF, arguing against the further use of amiodarone. The review article, which searched published reports over the past 30 years, finds no controlled studies administering amiodarone in WPW-AF [9, 16]. Furthermore, the review notes that out of ten patients with WPW-AF who had ventricular tachydysrhythmias after antidysrhythmic drug administration, seven of the cases involved IV amiodarone [16]. Fengler et al., in a case report, caution against the use of amiodarone as well, stating that IV amiodarone usage in WPW-AF is documented to cause ventricular rate acceleration leading to ventricular fibrillation [4]. Additionally, Schützenberger et al. [13] caution against the use of amiodarone in WPW-AF presenting a case report of an increased ventricular response secondary to accelerated conduction via the accessory pathway. Kappenburger et al. state in a study that though amiodarone is effective, it does not entirely prevent a rapid ventricular response in eight of ten patients with induced AF and a short effective refractory potential. The failure to prevent an increased ventricular response leads the study to call for the establishment of the safety of amiodarone in WPW-AF [5]. The findings support the notion that amiodarone may not be the safe pharmacological treatment of choice for rate control in WPW-AF [2, 4, 5, 13, 16].

This leads us to the question of procainamide and its effectiveness. A study of procainamide use by Li looked at 51 patients with WPW-AF. The study concludes that procainamide administration increases the antegrade effective refractory period and the intra-atrial conduction time significantly [6]. Schatz et al. support procainamide as the favored pharmacological treatment for patients with WPW-AF due to the ability to safely lengthen the effective refractory period [12]. Additionally, Fengler et al. [4] favor the use of procainamide in WPW-AF, stating procainamide prolongs the effective refractory period and slows antegrade and retrograde conduction in the AP. Procainamide has risks as well, including a significant side-effect profile, namely hypotension, QT-interval prolongation, and contraindications for patients with compromised cardiovascular function [3, 4].

Sotalol's effectiveness in rate control in patients with WPW-AF also calls for exploration. Madrid et al. [7] document conversion to a normal sinus rhythm in 12 of 22 patients who were administered sotalol. Additionally, the study finds no serious side effects and concludes that sotalol may be safe and effective [7]. Although sotalol is currently not available in the United States, it provides a pharmacological therapy option that warrants further study.

Amiodarone's relatively benign side-effect profile likely plays a role in the AHA recommendations. However, it is unclear whether this endorsement takes into consideration that amiodarone can cause ventricular fibrillation in a small but significant number of cases [2, 16], or that amiodarone is simply not efficacious in a number of wide-complex tachycardia cases [3, 8]. Despite procainamide's potential for WPW-AF control, it has significant side effects, including hypotension [3, 4]. This risk can be anticipated and mitigated with a slow infusion of procainamide plus an infusion of intravenous fluids. If hypotension continues, the infusion may be stopped, and the physician can move on to cardioversion. The small percentage of patients who go into ventricular fibrillation with amiodarone administration cannot be predicted or controlled by stopping an infusion. Therefore, the ability to stop a procainamide infusion upon recognition of undesirable side effects is an advantage over amiodarone.

Conclusion

Past studies paint an unclear picture of the clinical efficacy of amiodarone and procainamide in WPW-AF. None of the clinical studies noted above were formal, prospective, randomized, controlled trials. They had variable placebo and drug choices, significant variations in drug dosages and administration, and widely differing primary endpoints. Ultimately, we believe there is a strong need for a prospective, controlled trial of amiodarone versus procainamide for ventricular rate control in WPW-AF. Given this review, there is no available evidence that amiodarone is preferred over procainamide in rate control for WPW-AF, and may be dangerous.

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Conflict of interest None.

References

1. AHA (2005) American heart association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Part 7.3: Management of symptomatic bradycardia and tachycardia. Circ 112:IV-67–IV-77

2. Boriani G, Biffi M, Frabetti L et al (1996) Ventricular fibrillation after intravenous amiodarone in Wolff-Parkinson-White syndrome with atrial fibrillation. Am Heart J 131:1214–1216
3. Cummins RO, Hazinski MF (2006) The quest for a terminator. Ann Emerg Med 47:227–229
4. Fengler BT, Brady WJ, Plautz CU (2007) Atrial fibrillation in the Wolff-Parkinson-White syndrome: ECG recognition and treatment in the ED. Am J Emerg Med 25:576–583
5. Kappenberger LJ, Fromer MA, Steinbrunn W et al (1984) Efficacy of amiodarone in the Wolff-Parkinson-White syndrome with rapid ventricular response via accessory pathway during atrial fibrillation. Am J Cardiol 54:330–335
6. Li P (1991) Electrophysiological properties of atrial fibrillation with WPW syndrome and the role of procainamide in conversion. Chin J Cardiovasc Dis 19:65–66 123
7. Madrid AH, Moro C, Mańin Huerta EM et al (1992) Atrial fibrillation in Wolff-Parkinson-White syndrome: reversal of isoproterenol effects by sotalol. Pacing Clin Electrophysiol 15:2111–2115
8. Marill KA, deSouza IS, Nishijima DK et al (2006) Amiodarone is poorly effective for the acute termination of ventricular tachycardia. Ann Emerg Med 47:217–224
9. Pastor A, Almendral JM, Ormaetxe J et al (1993) Ventricular fibrillation during treatment of atrial fibrillation with intravenous amiodarone in patients with the WPW syndrome [abstract]. Eur Heart J 14(Suppl):294
10. Prystowsky EN, Benson DW Jr, Fuster V et al (1996) Management of patients with atrial fibrillation. A statement for healthcare professionals. From the subcommittee on electrocardiography and electrophysiology. American Heart Association. Circulation 93:1262–1277
11. Prystowsky EN, Katz AM (1998) Atrial fibrillation. In: Textbook of cardiovascular medicine. Lippincott-Raven. Philadelphia, Pennsylvania, p 1661
12. Schatz I, Ordog GJ, Karody R et al (1987) Wolff-Parkinson-White syndrome presenting in atrial fibrillation. Ann Emerg Med 16:574–578
13. Schützenberger W, Leisch F, Gmeiner R (1987) Enhanced accessory pathway conduction following intravenous amiodarone in atrial fibrillation. A case report. Int J Cardiol 16:93–95
14. Schützenberger W, Leisch F, Kerschner K et al (1989) Clinical efficacy of intravenous amiodarone in the short term treatment of recurrent sustained ventricular tachycardia and ventricular fibrillation. Br Heart J 62:367–371
15. Sheinman BD, Evans T (1982) Acceleration of ventricular rate by fibrillation associated with the Wolff-Parkinson-White syndrome. Br Med J (Clin Res Ed. 1981) 285:999–1000
16. Tijunelis MA, Herbert ME (2005) Myth: intravenous amiodarone is safe in patients with atrial fibrillation and Wolff-Parkinson-White syndrome in the emergency department. J Canad Assoc Emerg Phys 7:262–265