Original Article

Amiodarone vs. Digoxin for Ventricular-Rate Control in Patients with Atrial Fibrillation at the Emergency Department

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Objective: To compare an efficacy of amiodarone and digoxin in terms of rate control in patients with atrial fibrillation (AF) with rapid ventricular response at the emergency department.

Materials and Methods: The present study was a descriptive, retrospective study conducted at the University Hospital. The inclusion criteria were age over 18 years, presenting at the emergency room with AF and heart rate over 120 beats/min, and systolic blood pressure over 90 mmHg. There were four clinical outcomes examined including successful heart rate control, heart rate difference, treatment duration, and vital signs after treatment.

Results: During the study period, there were 147 patients who met the study criteria. Of those, 85 (57.83%) received amiodarone treatment. Regarding treatment outcomes, the amiodarone group had a significantly higher proportion of patients who achieved successful heart-rate control rate than the digoxin group (89.41% vs. 51.61%; p<0.001). Patients who received amiodarone were 1.4-times more likely to achieve a normal heart rate than digoxin (95% CI = 1.2 to 1.7 times, p-value <0.001). The two groups were comparable in terms of the other outcomes.

Conclusion: Intravenous amiodarone was able to control ventricular rate in AF patients better than digoxin. In settings in which access to intravenous antiarrhythmic agents is limited, amiodarone may be a potential alternative agent.

Keywords: Amiodarone, Digoxin, Ventricular rate, Outcomes

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Atrial fibrillation (AF) is a common cardiac arrhythmia treated at the emergency department. The admission rate of AF in the US was approximately 410,000 times in 2010 which was linear correlation from the year 1996[1]. AF has been shown to increase the risk for stroke and thromboembolism by six times[2,3]. The common presenting symptoms of AF at the emergency room are palpitations (52.8%) or chest pain (22.7%)[4]. Atrial fibrillation with rapid ventricular response is a common condition at the emergency department and requires treatment. Out of 371 patients with new onset AF, 301 patients (81.13%) were eligible for active management. A previous study also showed that AF patients with rapid ventricular response had a 91.8% admission rate from the emergency department[5].

There are several medications available that can be used to lower the ventricular rate in AF patients with rapid ventricular response conditions including metoprolol, diltiazem, and amiodarone[6]. A study conducted at a coronary care unit on 100 AF patients with rapid ventricular response who were randomly treated with either amiodarone or digoxin[7] found that patients' heart rates were significantly lower in the amiodarone group than in the digoxin group (p-value = 0.03). However, the study found comparable ventricular rates at 24 weeks[8]. The reduction in ventricular rate from baseline was 25% in patients treated with amiodarone vs. 27% in those treated with digoxin (p-value = 0.8). Both of these medications are intravenous drugs that are widely available in emergency departments in resource-limited settings particularly in developing countries. There has yet been no study conducted comparing these two medications in terms of rate control in patients with AF with rapid ventricular response at the emergency department.

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Materials and Methods

The present study was a descriptive, retrospective study conducted at the University Hospital Emergency Department. The inclusion criteria were age over 18 years,

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presenting at the emergency room with AF and heart rate over 120 beats/min, and systolic blood pressure over 90 mmHg. Patients who had a history of sick sinus syndrome, had received digoxin or amiodarone intravenously within 24 hours prior to admission, had received more than one heart rate-lowering agent, or were pregnant/breast feeding were excluded. The study period was between January and December 2016.

The authors reviewed the emergency medical records of all eligible patients. Baseline characteristics and clinical outcomes were recorded. There were four clinical outcomes examined including successful heart rate control, heart rate difference, treatment duration, and vital signs after treatment. Successful heart-rate control was defined as having a heart rate of 60 to 90 beats/min. Heart-rate difference was the difference between the baseline heart rate and heart rate after successful heart-rate control.

Sample size calculation

The sample size of the present study was calculated based on the results of a pilot study that included 20 patients with AF who received digoxin and amiodarone. The proportion of patients receiving each medication was 1: 1. Successful heart-rate control was achieved in 40% of patients in the digoxin and 60% in the amiodarone group. In order to achieve a power of 0.9 and confidence of 95% using a two-sided method, the required sample size was determined to be 140 patients.

Statistical analysis

Descriptive statistics was used to compare differences between the digoxin and amiodarone group. Either a Chi-square or Fisher Exact test was used to determine differences in categorical data, while an independent t-test or Wilcoxson rank-sum test was used for continuous data. For significant outcomes (defined by a *p*-value of less than 0.05), risk ratios and 95% confidence intervals (CIs) were also calculated.

Results

During the study period, there were 147 patients who met the study criteria. Of those, 85 (57.83%) received amiodarone treatment. The baseline characteristics of patients who received digoxin were comparable to those of the patients who received amiodarone with the exceptions of age, history of hypertension, and history of kidney disease (Table 1). The amiodarone group was older on average (73.5 vs. 67.8 years; *p*-value = 0.013), and had a higher proportion of patients with histories of hypertension (68.2% vs. 51.6%; *p*-value = 0.031) and kidney disease (24.7% vs. 11.3%; *p*-value = 0.031) than the digoxin group.

Regarding treatment outcomes, the amiodarone group had a significantly higher proportion of patients who achieved successful heart-rate control rate than the digoxin group (89.41% vs. 51.61%; $p<0.001$). Patients who received amiodarone were 1.4-times more likely to achieve a normal heart rate (95% CI = 1.2 to 1.7 times, *p*-value <0.001). The two groups were comparable in terms of the other outcomes such as heart rate and blood pressure after treatment (Table 2).

Discussion

The present study compared ventricular-rate control in AF patients treated with either digoxin or amiodarone

Table 1. Baseline characteristics of atrial fibrillation patients who received either digoxin or amiodarone treatment

Variables	Digoxin (n = 62)	Amiodarone (n = 85)	*p*-value
Age (year)	67.8±14.3	73.5±12.8	0.013
Male (n, %)	36 (42.4%)	49 (57.6%)	0.470
Body weight (kg)	60.3±14.5	60.7±12.7	0.901
Height (cm)	159.3±8.3	159.6±9.2	0.900
BMI (kg/m^2)	24.2±5.7	23.5±4.7	0.583
Vital signs before treatment			
Heart rate (per min)	148.6±14.7	146.6±16.4	0.450
Systolic BP (mmHg)	134.8±28.4	138.5±25.9	0.413
Diastolic BP (mmHg)	80.8±17.4	82.9±14.9	0.455
Body temperature (°C)	37.1±0.9	37.0±0.7	0.429
Hemoglobin (mg, %)	12.3±2.2	12.0±2.1	0.461
Underlying disease (n, %)			
Cardiac arrhythmia	26 (41.9%)	45 (52.9%)	0.125
Hypertension	32 (51.6%)	58 (68.2%)	0.031
Diabetes mellitus	20 (32.3%)	30 (35.3%)	0.419
COPD/Asthma	10 (16.1%)	8 (9.4%)	0.165
Congestive heart failure	6 (9.7%)	9 (10.6%)	0.543
Cerebrovascular disease	14 (22.6%)	13 (15.3%)	0.181
Coronary heart disease	16 (25.8%)	31 (36.5%)	0.117
Kidney disease	7 (11.3%)	21 (24.7%)	0.031
Others	29 (46.8%)	32 (37.7%)	0.174

Table 2. Treatment outcomes in atrial fibrillation patients who received either digoxin or amiodarone treatment

Outcomes	Digoxin (n = 62)	Amiodarone (n = 85)	*p*-value
Heart rate difference (per min) median (IQR)	41 (26)	47.5 (30)	0.137
Treatment duration in resuscitation room (min)	100 (120)	130 (340)	0.082
Vital signs after treatment			
Heart rate (per min)	101.9±13.8	96.2±18.0	0.115
Systolic BP (mmHg)	130.1±15.4	131.1±21.8	0.806
Diastolic BP (mmHg)	79.4±14.2	77.6±14.3	0.549
Successful heart-rate control	32 (51.61%)	76 (89.41%)	<0.001

at the emergency department (89.41% vs. 51.61%), a comparison that has been previously conducted only in the coronary care unit[7]. Although both amiodarone and digoxin lower ventricular rate by affecting at the atrioventricular node, we found that treatment with amiodarone resulted in better ventricular-rate control (89.41% vs. 51.61%). The heart rate outcome was slightly lower in the amiodarone group than in the digoxin group, but the treatment time in the emergency room was slightly longer in the amiodarone group than in the digoxin group. This may be due to amiodarone treatment administration requiring the use of an intravenous drip.

Although the ACC guidelines recommend intravenous beta-blockers as the first-line of treatment for ventricular rate control in AF patients[6], it is largely unavailable in developing countries. A study from one critical care unit found that intravenous metoprolol resulted in higher rates of ventricular-rate control than amiodarone and diltiazem in the overall ICU population[9] but that intravenous metoprolol had a comparable failure rate to that of amiodarone (but not diltiazem) in the non-cardiovascular ICU population (OR 1.19, CI 0.68 to 2.09, $p = 0.53$). This non-cardiovascular ICU population may be similar to that in our study at the emergency department. The main disadvantage of intravenous amiodarone was hypotension. Those who received amiodarone had a 3.34-times higher risk of requiring vasopressor therapy than those receiving metoprolol (*p*-value <0.01)[9].

The present study had some limitations. First, we did not study the dosages or regimens of the two medications. Second, the side effects of the medications were not recorded. Finally, the sample size was small and the study was conducted at a single-site referral university hospital. Finally, other causes or related conditions of AF were not explored such as obstructive sleep apnea or cardiovascular diseases[10-14].

Conclusion

Intravenous amiodarone was able to control ventricular rate in AF patients better than digoxin. In settings in which access to intravenous antiarrhythmic agents is limited, amiodarone may be a potential alternative agent.

What is already known on this topic?

Amiodarone and digoxin are the two common intravenous drugs in developing countries to reduce ventricular rate in AF.

What this study adds?

Intravenous amiodarone was able to control ventricular rate in AF patients better than digoxin at the emergency department.

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Conflicts of interest

The authors declare no conflicts of interest.

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การควบคุมการเต้นของหัวใจห้องล่างด้วยยา amiodarone เทียบกับ digoxin ในผู้ป่วยที่มีภาวะหัวใจห้องบนสั่นพลิ้วที่แผนกฉุกเฉิน

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วัตถุประสงค์: เพื่อเปรียบเทียบผลของยา amiodarone และ digoxin ในการควบคุมการเต้นของหัวใจห้องล่างในผู้ป่วยที่มีภาวะหัวใจห้องบนสั่นพลิ้วและมีอัตราการเต้นของหัวใจห้องล่างที่เร็วที่แผนกฉุกเฉิน

วัสดุและวิธีการ: การศึกษานี้เป็นการศึกษาย้อนหลังเชิงพรรณาโดยทำการศึกษาที่โรงพยาบาลมหาวิทยาลัย เกณฑ์คัดเข้าการศึกษาคือ ผู้ที่มีอายุมากกว่า 18 ปี มีอาการนำมาที่แผนกฉุกเฉินด้วยภาวะหัวใจห้องบนสั่นพลิ้วและมีอัตราการเต้นของหัวใจห้องล่างที่เร็วและมีระดับความดันโลหิตขณะบีบตัวมากกว่า 90 มม.ปรอท ผลการรักษาทางคลินิกประกอบไปด้วย 4 ปัจจัยได้แก่ อัตราการควบคุมการเต้นของหัวใจที่ได้ผล ความแตกต่างของอัตราการเต้นของหัวใจ ระยะเวลาในการรักษา และสัญญาชีพหลังการรักษา

ผลการศึกษา: ระหว่างระยะเวลาที่ทำการศึกษามีผู้ป่วยจำนวน 147 รายที่เข้าเกณฑ์การศึกษา มีผู้ป่วยจำนวน 87 ราย (ร้อยละ 57.83) ได้รับการรักษาด้วยยา amiodarone ในด้านผลการรักษาพบว่ายา amiodarone มีอัตราส่วนของผู้ป่วยที่สามารถควบคุมอัตราการเต้นของหัวใจได้ดีกว่ายาก digoxin อย่างมีนัยสำคัญทางสถิติ (ร้อยละ 89.41 และ 51.61; $p<0.001$ ผู้ป่วยที่ได้รับยา amiodarone สามารถมีอัตราการเต้นของหัวใจที่ปกติเป็น 1.4 เท่าเมื่อเทียบกับยา digoxin (95% CI = 1.2 ถึง 1.7 เท่า $p<0.001$). ผู้ป่วยทั้งสองกลุ่มมีผลการรักษาอื่น ๆ ที่ใกล้เคียงกัน

สรุป: ยา amiodarone ชนิดฉีดสามารถควบคุมอัตราการเต้นของหัวใจห้องล่างในผู้ป่วยภาวะหัวใจห้องบนสั่นพลิ้วได้ดีกว่ายา digoxin ในสถานการณ์ที่มีการใช้ยารักษาหัวใจเต้นผิดจังหวะชนิดฉีดที่จำกัด การให้ยา amiodarone เป็นยาทางเลือกที่มีแนวโน้มการรักษาที่ดี