Heart Surgery Forum 2023; 26(5): E463–E469
doi: 10.59958/hsf.5683

Article

Effects of Moracizine Combined with Metoprolol on Hemodynamic Indices of the Left Atrium and Quality of Life in Patients with Atrial Fibrillation

Gongzhu Han[1], Ting Fu[2], Yichao Zhang[3,*]

[1]Department of Cardiology, Jiaozhou Central Hospital of Qingdao, 266300 Jiaozhou, Shandong, China
[2]Pharmaceutical Department, Qingdao Hospital, University of Health and Rehabilitation Sciences (Qingdao Municipal Hospital), 266000 Qingdao, Shandong, China
[3]Department of Emergency Medicine, Affiliated Central Hospital of Shandong First Medical University, 250000 Jinan, Shandong, China
*Correspondence: Zhangyichao112@163.com (Yichao Zhang)

Submitted: 18 April 2023 Revised: 24 August 2023 Accepted: 27 August 2023 Published: 7 October 2023

Abstract

Background: Drugs are the first choice of treatment for atrial fibrillation (AF), but there is currently a lack of efficient drug treatment options. The aim of this study was to investigate a combination drug treatment plan which may serve as a reference for the treatment of AF. **Methods**: A total of 316 AF patients admitted to Jiaozhou Central Hospital in Qingdao from October 2020 to October 2022 were selected for this retrospective study. They were divided into a control group (CG, metoprolol, n = 156) and an observation group (OG, moracizine combined with metoprolol, n = 160) based on the treatment they received. The CG and OG groups were compared for clinical efficacy, occurrence of AF, cardiac output (CO), cardiac indexes (CI), stroke volume (SV), stroke indexes (SI) and improvement in QOL. **Results**: The OG had a better effective rate of treatment, higher levels of CO, CI, SV and SI, and higher QOL scores compared to the CG, as well as a lower AF recurrence rate and AF burden (all $p < 0.05$). **Conclusion**: Moracizine combined with metoprolol is an effective treatment for AF patients. This drug combination was found to reduce the AF recurrence rate and burden in AF patients, and to improve their hemodynamic indices and QOL.

Keywords

moracizine; metoprolol; atrial fibrillation; hemodynamic indices; quality of life

Introduction

Atrial fibrillation (AF) is a common arrhythmia that accounts for about one third of hospital patients with arrhythmia. AF is associated with a high disability rate and high mortality [1]. When AF occurs, the normal atrial electrical activity becomes disordered and patients experience a loss of normal effective contraction and relaxation, a disordered heart rate, and partial loss of atrial ejection function, thereby leading to hemodynamic impairment [2,3]. Due to the loss of atrial contraction during AF, the blood in the atrium is prone to stasis. The resulting deciduous thrombus can be carried by the blood throughout the body, causing cerebral infarction, limb artery embolism, and threatening the physical health and life of patients. Medical treatment for AF is therefore vital so that patients can restore and maintain sinus rhythm, control ventricular rate, and thus prevent the complications of thromboembolism [4]. Moracizine is characterized by moderate expansion of coronary artery, spasmolysis and anti-M cholinergic effect. The commonly used moracizine has an obvious antitachyarrhythmia effect and is used to treat atrial premature beat, ventricular premature beat, paroxysmal tachycardia, AF, and atrial flutter. Moracizine is a class I antiarrhythmic agent with low toxicity, mild side effects, and good tolerance. Its therapeutic indexes exceed those of quinidine and procaine amine. The latter drugs can accelerate the second and third phases of repolarization, thereby shortening the action potential duration and prolonging the effective refractory period. A study of moracizine treatment for atrial arrhythmias found that it significantly reduced the incidence of AF and of AF burden without affecting the sinus rhythm [5]. Metoprolol is a selective $\beta 1$ receptor blocker that can reduce the heart rate and cardiac output (CO) at rest and during exercise, reduce blood pressure, and slow atrioventricular conduction to decrease the sinus rhythm [6]. Metoprolol is effective in the treatment of AF patients, as observed by anticoagulation, control of ventricular rate, and transformation to sinus heart rate, which improves heart rate variability and cardiac function [7]. However, there are few clinical studies on the combination of moracizine and metoprolol for the treatment of AF, and the effects of this combination on patient symptoms and hemodynamics are still unclear. The aim of this study was therefore to evaluate the efficacy of combined moracizine and metoprolol treatment for AF using multiple indicators, with the results serving as a reference for the clinical treatment of AF.

Materials and Methods

Study Design

A total of 316 AF patients admitted to Jiaozhou Central Hospital in Qingdao, China, from October 2020 to October 2022 were selected for this retrospective study. They were divided into the control group (CG, metoprolol treatment, n = 156) and the observation group (OG, combined moracizine and metoprolol treatment, n = 160) according to the treatment received. The therapeutic effects in the two treatment groups were compared and analyzed, thus allowing evaluation of the mechanism of action the moracizine and metoprolol combination. Technical details for this study are shown in Fig. 1.

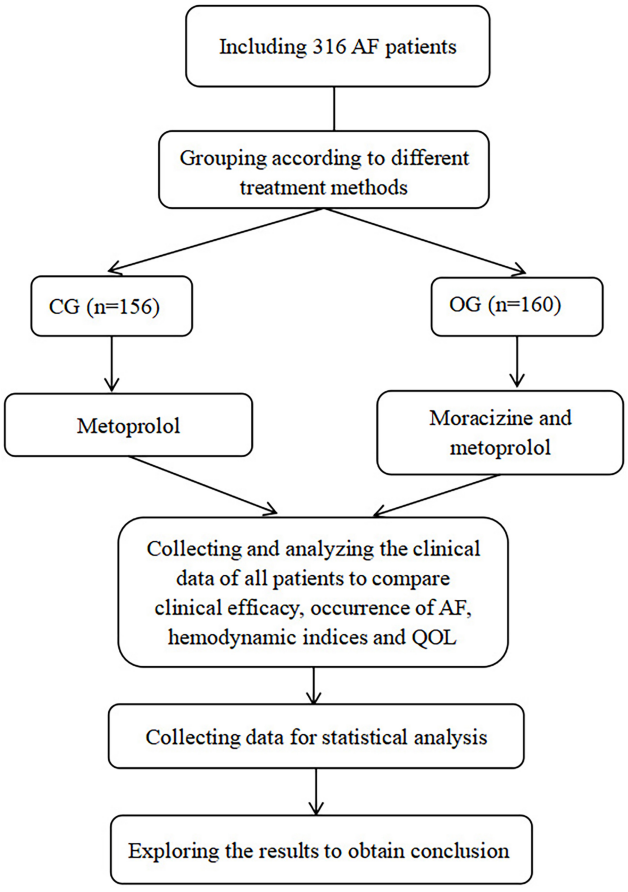

Fig. 1. Study flowchart. AF, atrial fibrillation; CG, control group; OG, observation group; QOL, quality of life.

Inclusion and Exclusion Criteria

The inclusion criteria were: (1) patients diagnosed with AF by electrocardiogram, clinical symptoms and physical examination; (2) patients with complete clinical data; (3) patients with clinical symptoms such as palpitation, shortness of breath, and precordial pain. The exclusion criteria were: (1) patients with severe dysfunction in heart, liver and kidney; (2) patients who could not cooperate with the study requirements due to severe mental illness; (3) patients with allergy or contraindication to the drugs used in the study; (4) patients with severe cerebrovascular diseases; (5) pregnant or lactating women; (6) patients with immune system diseases and coagulation disorders; (7) patients who withdrew from the study due to uncontrollable factors; and (8) patients who did not take the necessary drugs used in the study.

Patients and their family were informed of the purpose and process of this study and gave signed informed consent. This study conformed to the principles of the Declaration of Helsinki (2013) [8] and was approved by the ethics committee of Jiaozhou Central Hospital, Qingdao (approval No.: 20190846).

Methods

All patients received conventional oral therapy with metoprolol (manufacturer: AstraZeneca Pharmaceutical Co., Ltd.; NMPA approval No.: H32025391; specification: 25 mg × 20 tablets; No.: 363; origin: Shanghai, China). One tablet of metoprolol was taken orally twice per day. Patients in the OG received moracizine in addition (manufacturer: Shenyang Shengyuan Pharmaceutical Co., Ltd.; NMPA approval No.: H20056627; specification: 50 mg; No.: 295; origin: Shenyang, Liaoning province, China). One tablet of moricizine were taken orally three times per day and at 8-hour intervals. In later stages, The dosage of Moricizine was appropriately increased according to the patients' condition in the later period, and to a maximum of 900 mg per day, with continuous treatment for 3 months.

Observation Indexes

The baseline data for the two groups were compared. These included gender, age, body mass index (BMI), type of AF, average heart rate during AF, primary diseases, education level, and place of residence.

The clinical efficacy in both groups was compared, with the evaluation criteria reported as follows. If clinical symptoms and signs disappeared or largely disappeared, and the onset frequency of AF was reduced by >90% compared to before treatment, the treatment was considered to be "clearly effective". If clinical symptoms and signs were significantly improved, and the onset frequency of AF was reduced by >50% compared to before treatment, the treatment was considered to be "effective". If clinical symptoms and signs were not improved and the onset frequency of AF was reduced by <50% or showed no improvement compared to before treatment, the treatment was considered "ineffective". The overall effective rate was calculated as: clearly effective cases + effective cases/total cases × 100%.

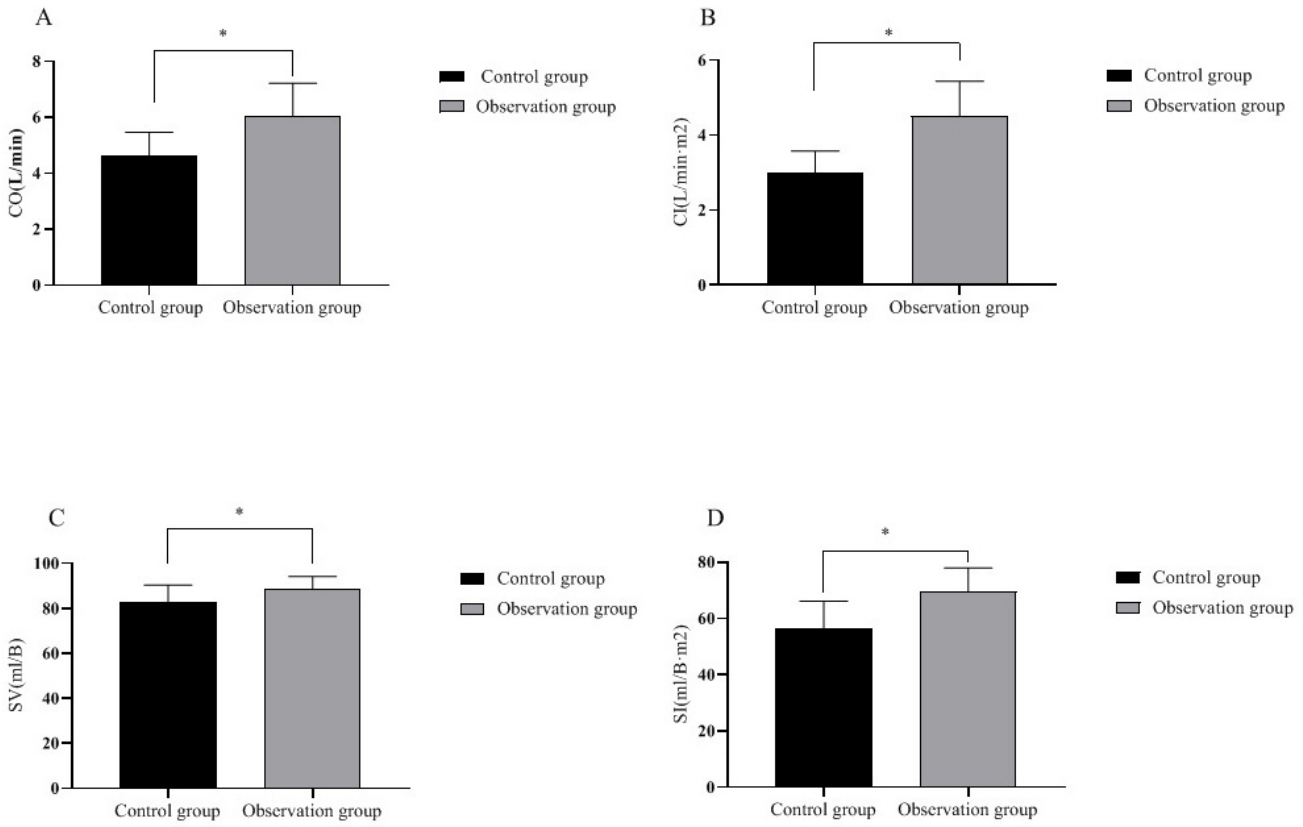

Fig. 2. Comparison of hemodynamic indices between CG and OG following treatment ($\bar{x} \pm$ SD). (A) Comparison of CO. (B) Comparison of CI. (C) Comparison of SV. (D) Comparison of SI. CO, cardiac output; CI, cardiac indexes; SV, stroke volume; SI, stroke indexes. "*" indicated a significant difference between the two groups, $p < 0.05$.

To determine AF, all patients were evaluated with a 24 h dynamic electrocardiogram detector (manufacturer: Shandong Shengdong Medical Technology Co., Ltd.; model: DYX-1A; No.: 10076901601501; origin: Jinan, Shandong province, China). The occurrence of AF in the two groups was recorded, allowing comparison of the AF recurrence rate and AF burden.

Hemodynamic indices were evaluated using a non-invasive hemodynamic detector (manufacturer: Guangdong Kangbeisite Medical Technology Co., Ltd.; model: CSM3100; No.: 20152210493; origin: Guangzhou, Guangdong province, China). CO, cardiac indexes (CI), stroke volume (SV) and stroke indexes (SI) were compared between the two groups.

The quality-of-life (QOL) scale (SF-36) [9] was used to evaluate patient QOL. SF-36 covers 8 aspects: physiological function, physiological role, physical pain, general health status, vigor, social function, emotional function and mental health. It has a total of 36 questions and the maximum score of each dimension is 100 points. The higher the score, the better the QOL.

Statistical Methods

The data processing software used in this study was SPSS20.0 (IBM Corp., Armonk, NY, USA). GraphPad Prism 7 (San Diego, CA, USA) was used to plot the data. Numerical data and measurement data were tested by χ^2 and t test, and presented as [n (%)] or as mean $\pm$ standard deviation ($\bar{x} \pm$ SD). Differences between groups were considered to be statistically significant when $p < 0.05$.

Results

Comparison of Baseline Data between CG and OG

As shown in Table 1, no significant differences in any of the baseline data were observed between the two groups ($p > 0.05$).

Comparison of Clinical Efficacy between CG and OG

As shown in Table 2, the overall effective rate of treatment was significantly higher in OG compared to CG ($p < 0.05$).

Table 1. Comparison of baseline data between CG and OG [n (%)].

Index	CG (n = 156)	OG (n = 160)	χ^2/t	p
Gender			0.024	0.876
Male	93 (59.62)	94 (58.75)		
Female	63 (40.38)	66 (41.25)		
Average age (years)	59.03 ± 9.48	59.38 ± 8.99	1.379	0.168
BMI ($\bar{x}$ ± SD, kg/m^2)	21.64 ± 1.38	21.39 ± 1.58	1.470	0.142
Blood pressure levels				
Systolic pressure (mmHg)	126.17 ± 15.55	125.83 ± 14.61	0.201	0.841
Diastolic pressure (mmHg)	86.24 ± 8.70	87.01 ± 9.10	0.767	0.443
Heart rate (times/min)	85.65 ± 11.68	85.82 ± 11.82	0.125	0.901
Types of AF			1.232	0.540
Primary	45 (28.85)	51 (31.88)		
Paroxysmal	74 (47.44)	66 (41.25)		
Persistent	37 (23.72)	43 (26.88)		
Average heart rate during AF ($\bar{x}$ ± SD, times/min)	128.03 ± 15.31	127.13 ± 16.77	0.498	0.619
Primary disease			0.312	0.958
Hypertension	51 (32.69)	53 (33.13)		
Diabetes mellitus	39 (25.00)	41 (25.63)		
Coronary heart disease	34 (21.79)	37 (23.13)		
None	32 (20.52)	29 (18.13)		
Education level			0.119	0.730
College and above	74 (47.44)	79 (49.38)		
High school or below	82 (52.56)	81 (50.63)		
Place of residence			0.108	0.743
Urban area	76 (48.72)	75 (46.88)		
Rural area	80 (51.28)	85 (53.13)		

BMI, body mass index.

Table 2. Comparison of clinical efficacy between CG and OG [n (%)].

Group	Cases	Clearly effective	Effective	Ineffective	Overall effective
CG	156	61 (39.10)	63 (40.38)	32 (20.51)	124 (79.49)
OG	160	70 (43.75)	76 (47.50)	14 (8.75)	146 (91.25)
χ^2					8.828
p					0.012

Comparison of AF between CG and OG

There was no significant difference in the duration of AF between CG and OG ($p > 0.05$). However, as shown in Table 3, the recurrence rate of AF and the AF burden were both significantly lower in OG than in CG ($p < 0.05$).

Comparison of Hemodynamic Indices between CG and OG

As shown in Fig. 2 and Table 4, the levels of CO, CI, SV and SI following treatment were higher in the OG than in the CG ($p < 0.05$).

Comparison of SF-36 Score between CG and OG

As shown in Table 5, the OG had significantly higher QOL scores than the CG following treatment ($p < 0.05$).

Discussion

AF refers to the loss of orderly atrial electrical activity, which is replaced by rapid and disorderly fibrillation waves. This serious disorder of atrial electrical activity has a high clinical incidence, with the main pathophysiological characteristics being a disordered ventricular rate, impaired cardiac function, and atrial mural thrombosis [10–12]. The incidence of AF increases significantly with age [13], affecting 10% of people aged > 75 years. AF is the second most common arrhythmia after ventricular premature beat. The clinical manifestations of AF include palpitations, vertigo, chest discomfort and shortness of breath, all of which seriously impact the patients' QOL and physical health [14–16]. Moracizine is a commonly used antiarrhythmic drug that inhibits the rapid internal flow of Na^+, affects membrane stabilization, shortens 2-phase and 3-phase repolarization and action potential time, and reduces the effective

Table 3. Comparison of AF in CG and OG (n, $\bar{x} \pm$ SD).

Group	Cases	Duration of AF	Recurrence rate of AF (%)	AF burden (%)
CG	156	3.51 ± 2.00	44 (28.21)	8.08 ± 1.83
OG	160	3.42 ± 1.81	21 (13.13)	6.84 ± 1.86
χ^2/t		0.433	10.994	6.005
p		0.666	0.001	<0.001

Table 4. Comparison of hemodynamic indices between CG and OG ($\bar{x} \pm$ SD).

Observation index	Time	CG	OG	t	p
CO (L/min)	Before treatment	2.88 ± 0.24	2.92 ± 0.36	1.341	0.181
	After treatment	4.65 ± 0.81	6.07 ± 1.15	12.619	<0.001
CI (L/min·m^2)	Before treatment	1.93 ± 0.22	2.02 ± 0.30	1.591	0.113
	After treatment	3.01 ± 0.57	4.51 ± 0.93	17.309	<0.001
SV (mL/B)	Before treatment	52.81 ± 6.96	53.29 ± 7.39	0.589	0.556
	After treatment	83.04 ± 7.32	88.89 ± 5.20	8.209	<0.001
SI (mL/B·m^2)	Before treatment	42.93 ± 4.44	43.49 ± 3.49	1.260	0.209
	After treatment	56.34 ± 9.81	69.69 ± 8.28	13.089	<0.001

Table 5. Comparison of SF-36 scores between CG and OG ($\bar{x} \pm$ SD).

Evaluation indicators	Times	CG	OG	t	p
Physiological function	Before treatment	50.07 ± 6.38	50.52 ± 4.30	0.734	0.463
	After treatment	64.38 ± 5.96	82.79 ± 5.94	27.502	<0.001
Physiological role	Before treatment	54.87 ± 4.90	55.28 ± 5.44	0.703	0.483
	After treatment	79.42 ± 6.70	89.16 ± 4.14	15.580	<0.001
Physical pain	Before treatment	52.60 ± 4.21	53.43 ± 5.21	1.541	0.124
	After treatment	67.23 ± 5.57	83.06 ± 6.30	23.639	<0.001
General health status	Before treatment	58.68 ± 4.47	58.79 ± 5.19	0.198	0.843
	After treatment	80.47 ± 4.44	88.06 ± 5.71	13.176	<0.001
Vigor	Before treatment	55.73 ± 4.33	55.51 ± 4.65	0.431	0.667
	After treatment	75.78 ± 5.34	86.86 ± 4.26	20.404	<0.001
Social function	Before treatment	54.24 ± 5.44	53.94 ± 5.99	0.456	0.648
	After treatment	79.31 ± 5.55	90.59 ± 3.56	21.558	<0.001
Emotional function	Before treatment	54.70 ± 4.95	55.16 ± 4.37	0.883	0.378
	After treatment	70.44 ± 6.06	86.58 ± 6.07	23.644	<0.001
Mental health	Before treatment	57.10 ± 4.34	57.16 ± 4.39	0.135	0.893
	After treatment	71.05 ± 6.58	86.69 ± 5.11	23.638	<0.001

refractory period, thereby improving arrhythmia. This drug is often used to treat arrhythmia in patients with coronary heart disease, angina pectoris, hypertension, etc. It has significant therapeutic effects, minor side effects, and good safety. Metoprolol is a β-blocker that reduces the heart rate, prolongs diastolic time, fills the left ventricle, increases diastolic volume in the terminal phase, and effectively alleviates myocardial ischemia and hypoxia [17,18]. In the present study, the clinical efficacy of moracizine combined with metoprolol for the treatment of AF patients was investigated in order to provide additional data to help guide clinical practice.

It was previously reported that metoprolol combined with amiodarone for the treatment of patients with acute myocardial infarction and arrhythmia could improve the clinical efficacy and reduce the symptoms of palpitation and chest tightness caused by excessive heart rate [19]. In the present study, the overall rate of effective treatment was found to be significantly higher in the OG than in the CG ($p < 0.05$), indicating the moracizine and metoprolol combination was superior to metoprolol alone. If AF, atrial flutter and other symptoms occur within 3 months after treatment and last for 30 s or more, the AF condition is considered to be recurrent. Both the incidence of AF and the AF burden were lower in the OG than in the CG ($p < 0.05$), suggesting the moracizine and metoprolol combination was effective at reducing these conditions. This drug combination may therefore have a significant and synergistic inhibitory effect on the occurrence of AF. Trimetazidine can protect cardiomyocytes from injury and maintain the balance of myocardial blood supply and oxygen supply. Metoprolol can inhibit myocardial contraction to exert a hypotensive

effect, inhibit endogenous catechol secretion, while also reducing myocardial oxygen consumption, heart rate, AF burden and the incidence of AF [20–22]. In AF patients with a high heart rate, the ventricle does not fully fill with blood and cardiac function decreases by approximately 25% due to the loss of atrial function, resulting in a smaller cardiac ejection volume and hemodynamic disorders [23]. The occurrence of AF has a major impact on hemodynamics, causing inconsistent atrial and ventricular activity, decreased heart pump function, and adverse phenomena such as palpitation, amaurosis and syncope [24]. It is therefore necessary to convert AF into sinus rhythm and to prevent AF recurrence, thereby ensuring the stability of blood flow after treatment. In the present study, hemodynamic indices in AF patients were improved by treatment with moracizine and metoprolol (OG), with the levels of CO, CI, SV and SI all being higher than those in the CG ($p < 0.05$). Therefore, treatment with this drug combination promotes blood circulation in the coronary artery and peripheral arteries, reduces systolic pressure, relieves cardiac afterload, increases cardiac output, and improves hemodynamics. Moreover, the QOL score was higher in the OG than the CG ($p < 0.05$), further confirming the efficacy of this drug combination for the treatment of AF. Amiodarone and propafenone are more commonly used in the clinical treatment of AF, but these drugs have a higher withdrawal rate during treatment, mostly discounted in the form of doctor's prescription. After intravenous injection of antiarrhythmic drugs such as amiodarone, 4.9% of patients have cardiac conduction block or bradycardia, and 16% of patients have hypotension [25]. Therefore, doctors usually evaluate the relevant risks before prescribing these drugs. In the current study, patients treated with the moracizine and metoprolol combination showed better treatment effects, a lower recurrence rate for AF, and good hemodynamic improvement. In summary, the combination of these two drugs can be used for effective treatment of AF patients.

Although many drugs are available for the clinical treatment of AF, including amiodarone and propafenone, few studies have examined the use of moracizine combined with metoprolol. This novel study examined the combination of these drugs to treat AF patients. The observed improvements in clinical symptoms, the positive effects on hemodynamic indexes, and the improved QOL scores provide new evidence to help guide the treatment of AF patients.

There are some limitations with this study. The retrospective study design and the recruitment of patients from the same hospital may have biased the results. Multi-center, prospective studies are needed to further examine the mechanism of action of the moracizine and metoprolol drug combination. In future research, more parameters also should be studied to confirm the effects of this drug combination.

Conclusion

In conclusion, the treatment of AF patients with moracizine and metoprolol can improve their clinical condition, improve hemodynamic parameters, and enhance their quality of life, thus offering a new treatment option for AF.

Availability of Data and Materials

Data to support the findings of this study are available on reasonable request from the corresponding author.

Author Contributions

GH and YZ contributed to the concept and designed the research study. GH and TF performed the research. YZ and TF provided help and advice on the experiments. GH and YZ contributed to the analysis and interpretation of the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study conforming to the principles of Declaration of Helsinki (2013) [8] has been approved by the ethical committee of Jiaozhou Central Hospital of Qingdao (approval No.: 20190846).

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Harskamp RE, Lucassen WAM, Lopes RD, Himmelreich JCL, Parati G, Weert HCPMV. Risk of stroke and bleeding in relation

to hypertension in anticoagulated patients with atrial fibrillation: a meta-analysis of randomised controlled trials. Acta Cardiologica. 2022; 77: 191–195.
[2] Aldana-Bitar J, Moore J, Manubolu VS, Dahal S, Verghese D, Lakshmanan S, *et al*. Plaque Progression Differences Between Apixaban and Rivaroxaban in Patients With Atrial Fibrillation Measured With Cardiac Computed Tomography and Plaque Quantification. American Journal of Therapeutics. 2023; 30: e313–e320.
[3] Nielsen PB, Søgaard M, Jensen M, Ording AG, Lip GY. Comparative effectiveness and safety of edoxaban versus warfarin in patients with atrial fibrillation: A nationwide cohort study. International Journal of Stroke. 2022; 17: 536–544.
[4] Benz AP, Healey JS, Chin A, Commerford P, Marsden T, Karthikeyan G, *et al*. Stroke risk prediction in patients with atrial fibrillation with and without rheumatic heart disease. Cardiovascular Research. 2022; 118: 295–304.
[5] Zou T, Chen Q, Chen C, Liu G, Ling Y, Pang Y, *et al*. Moricizine prevents atrial fibrillation by late sodium current inhibition in atrial myocytes. Journal of Thoracic Disease. 2022; 14: 2187–2200.
[6] Nuñez Cruz S, DeMott JM, Peksa GD, Slocum GW. Evaluation of the blood pressure effects of diltiazem versus metoprolol in the acute treatment of atrial fibrillation with rapid ventricular rate. The American Journal of Emergency Medicine. 2021; 46: 329–334.
[7] McGrath P, Kersten B, Chilbert MR, Rusch C, Nadler M. Evaluation of metoprolol versus diltiazem for rate control of atrial fibrillation in the emergency department. The American Journal of Emergency Medicine. 2021; 46: 585–590.
[8] World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013; 310: 2191–2194.
[9] Halperin LF, Lee MK, Liew J, Lauck S, Kong D, Krahn AD, *et al*. Anticoagulation for Patients With Atrial Fibrillation and End-Stage Renal Disease on Dialysis: A National Survey. The Canadian Journal of Cardiology. 2021; 37: 924–928.
[10] Jin C, Cui C, Seplowe M, Lee KI, Vegunta R, Li B, *et al*. Anticoagulation for Atrial Fibrillation: A Review of Current Literature and Views. Cardiology in Review. 2022. (online ahead of print)
[11] Zhao Y, Krupadev V, Dagher L, Mahnkopf C, Sohns C, Sehner S, *et al*. Pharmacological rhythm versus rate control in patients with atrial fibrillation and heart failure: the CASTLE-AF trial. Journal of Interventional Cardiac Electrophysiology. 2021; 61: 609–615.
[12] Fanaroff AC, Li S, Marquis-Gravel G, Giri J, Lopes RD, Piccini JP, *et al*. Atrial Fibrillation and Coronary Artery Disease: A Long-Term Perspective on the Need for Combined Antithrombotic Therapy. Circulation. Cardiovascular Interventions. 2021; 14: e011232.
[13] Eyuboglu M. Frontal plane QRS-T angle in the monitoring of intravenous amiodarone infusion for pharmacological cardioversion of acute atrial fibrillation. Journal of Clinical Pharmacy and Therapeutics. 2021; 46: 731–737.
[14] Marum AA, Araujo Silva B, Bortolotto AL, Pedreira GC, Tessarolo Silva F, Medeiros SA, *et al*. Pulmonary Delivery of Metoprolol Reduces Ventricular Rate During Atrial Fibrillation and Accelerates Conversion to Sinus Rhythm. Journal of Cardiovascular Pharmacology. 2020; 75: 135–140.
[15] Vinereanu D, Spinar J, Pathak A, Kozlowski D. Role of Metoprolol Succinate in the Treatment of Heart Failure and Atrial Fibrillation: A Systematic Review. American Journal of Therapeutics. 2020; 27: e183–e193.
[16] Compagner CT, Wysocki CR, Reich EK, Zimmerman LH, Holzhausen JM. Intravenous metoprolol versus diltiazem for atrial fibrillation with concomitant heart failure. The American Journal of Emergency Medicine. 2022; 62: 49–54.
[17] DiNicolantonio JJ, Beavers CJ, Menezes AR, Lavie CJ, O'Keefe JH, Meier P, *et al*. Meta-analysis comparing carvedilol versus metoprolol for the prevention of postoperative atrial fibrillation following coronary artery bypass grafting. The American Journal of Cardiology. 2014; 113: 565–569.
[18] Hargrove KL, Robinson EE, Lusk KA, Hughes DW, Neff LA, Fowler AL. Comparison of sustained rate control in atrial fibrillation with rapid ventricular rate: Metoprolol vs. Diltiazem. The American Journal of Emergency Medicine. 2021; 40: 15–19.
[19] Liu Y, Hong Y. Amiodarone vs. metoprolol succinate in HFrEF complicated with persistent atrial fibrillation with rapid ventricular response: A prospective observational study. Frontiers in Cardiovascular Medicine. 2023; 9: 1029012.
[20] Niforatos JD, Ehmann MR, Balhara KS, Hinson JS, Ramcharran L, Lobner K, *et al*. Management of atrial flutter and atrial fibrillation with rapid ventricular response in patients with acute decompensated heart failure: A systematic review. Academic Emergency Medicine. 2023; 30: 124–132.
[21] Jing Y, Xu J, Chen B, Xia D, Xia D, Tian Y, *et al*. Superior mesenteric artery embolism after radiofrequency ablation in regularly anticoagulated patients with paroxysmal atrial fibrillation: a case report. BMC Cardiovascular Disorders. 2023; 23: 56.
[22] Chen J, Zhao Y, Ma C, Du X, He Y, Li H. Left atrial deformation and risk of transient ischemic attack and stroke in patients with paroxysmal atrial fibrillation. Medicine. 2023; 102: e32745.
[23] Boivin-Proulx LA, Potter BJ, Dorais M, Perreault S. Evolution of and Evidence-Practice Gaps in Antithrombotic Management of Atrial Fibrillation Patients After Percutaneous Coronary Intervention. CJC Open. 2022; 5: 15–23.
[24] Ken-Opurum J, Srinivas SS, Park S, Charland S, Revel A, Preblick R. Clinical and economic outcomes associated with use of anti-arrhythmic drugs versus ablation in atrial fibrillation. Journal of Comparative Effectiveness Research. 2023; 12: e230065.
[25] Colunga Biancatelli RM, Congedo V, Calvosa L, Ciacciarelli M, Polidoro A, Iuliano L. Adverse reactions of Amiodarone. Journal of Geriatric Cardiology. 2019; 16: 552–566.