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# *A case study of hypotensive shock induced by metoprolol combined with propafenone hydrochloride*

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***Abstract:*** In order to further clarify the accuracy of drug interactions. Clinicians participated in the treatment and rescue of a patient with hypotensive shock caused by the combination of metoprolol and propafenone hydrochloride. According to the patient's condition, they read relevant references and combined pharmaceutical knowledge, clinical thinking and evidence-based medicine principles to provide basic research on the correlation between drug interactions. Resultly, we get a clear understanding of the interactions between drugs, which can provide clinicians with accurate medication plans, provide patients with individualized pharmaceutical care, and ensure safe and rational drug use by clinicians.

## 1. Introduction

According to many domestic and foreign literature reports, the use of multi-drug combination therapy is a common phenomenon in cardiovascular diseases [1], and the combination of some drugs will lead to drug interaction. Drug interactions (DI) refer to the phenomenon of changes in the physicochemical, pharmacokinetic or pharmacodynamic properties of the original drugs when two or two drugs are used simultaneously or in combination. Although multidrug therapy increases pharmacokinetic or pharmacodynamic properties, it also potentially increases the risk of drug interactions [2]. This article reports a case of hypotensive shock caused by metoprolol and propafenone hydrochloride during hospitalization, in order to provide reference for clinicians.

## 2. Case data

The patient, surnamed Wang, female, 74 years old, was admitted to the cardiology Department of the Affiliated Hospital of Shaanxi University of Chinese Medicine on December 25, 2021 due to "paroxyetic palpitation and shortness of breath for more than 3 years, aggravated by 6 hours". He has a history of "hypertension" for 40 years, and his maximum blood pressure can reach 220/120mmHg. He takes fosinopril, amlodipine besylate tablets and Metoprolol tartrate sustained-release tablets regularly, and his blood pressure is generally controlled. History of "paroxysmal atrial fibrillation" for 1 year, rivaroxaban tablets taken regularly recently; He has a history of chronic cholecystitis. Previous medication history: fosinopril tablet (10mg, qd, po), amlodipine besylate tablet (5mg, qd,

po), rivaroxaban tablet (20mg, qd, po), metoprolol tartrate tablet (betalock 25mg, tid, po), atorvastatin calcium tablet (20mg, qd, po), denied food and drug allergy history. Admitted to hospital for physical examination: body temperature 36.8℃, pulse 78 times/min, respiration 20 times/min, blood pressure 158/85mmHg, clear mind, clear breathing sound in both lungs, and no dry or wet rales were heard. There was no uplift in the precardiac area, the apex beat was located at the left midclavicular line of the fifth intercostal space, no uplifting beat was touched, the boundary of cardiac dullness was normal, the rhythm was consistent, and the heart sound was normal, no pathological murmurs were heard in the auscultation area of each valve, and no acardiac fricative sound was included. After admission, ECG was checked: sinus rhythm, occasional supracentricular premature beat, occasional ventricular premature beat. Important clinical information and duration of treatment during hospitalization are shown in Table 1.

Table 1: Important clinical information and duration

| Hospital Stays | Vital Signs | Cure |
|---|---|---|
| Admission d1 | Improve blood, urine, stool, coagulation, kidney function, electrolytes, lipids, BNP, heart B-ultrasound,dynamic electrocardiogram, ambulatorized blood pressure and other routine examinations. | Treatment of atrial fibrillation with ABC protocol: anticoagulation, control of symptoms, control of risk factors (fosinopril, amlodipine, rivaroxaban, metoprolol, atorvastatin); TCM mainly focuses on nourishing the heart qi and promoting blood circulation and collaterals. |
| Admission d3 | BP: 153/84mmHg, heart rate 72 times/min, electrolyte determination, chest CT examination. | Potassium chloride injection (3g, tid, po), cardiopine (150mg, tid, po); Stop using betaloc for metoprolol succinate sustained-release tablets (23.75mg, TID, PO), and forsinpril to 10mg, 2 times a day, orally. |
| Admission d5 | The blood pressure was 168/89 MMHG and the heart rate was 77 beats/min. Holter monitoring showed 336 atrial premature beats, 1 paroxysmal atrial tachycardia and 2 ventricular premature beats in 24 hours. Ambulatory blood pressure was 158/77 MMHG at night and 160/107 MMHG at day. | Amlodipine besylate was discontinued and replaced with oral nifedipine sustained-release tablets (I) 20mg, bid. |
| Admission d6 | Blood pressure: 125/78 MMHG, heart rate 72 beats/min. | Subsequent drug therapy (fosinopril + nifedipine + metoprolol succinate + rivaroxaban + atorvastatin + arrhythmiapine) |
| Admission d6(20: 00) | The patient was given nifedipine 20mg and fosinopril 10mg orally at 18:30. The blood pressure was 84/48mmHg. Auscultation showed that the lungs were negative and the heart sounds were low and blunt. Blood glucose level was 9.3mmol/L.Electrocardiogram showed sinus bradycardia with a heart rate of 40 beats/min. | 5% glucose 250ml and Shengmai injection 60ml were given intravenously. Electrocardiogram monitoring and oxygen inhalation were given at the same time. |
| Admission d6(20: 10) | The symptoms were not relieved, and the BP was 63/39 mmHg. | 5% glucose 250ml+ Shengmai injection 60ml intravenous drip, 5% glucose 40ml+ dopamine hydrochloride injection 100mg 5ml/h micro-pump injection (dose adjustment according to blood pressure). |
| Admission d6(20: 50) | The patient developed nausea and vomiting with a BP of 64/57 MMHG. Slight relief of symptoms. | The dose of dopamine was gradually increased to 12ug/Kg/min, and the blood pressure did not rise significantly. Then 5% glucose injection 46ml+ norepinephrine injection 8mg 5ml/h micropump injection (the dosage was adjusted according to blood pressure). |
| Admission d6(21: 00) | The blood pressure was 110/63 mmHg, and the electrocardiogram showed sinus rhythm with a heart rate of 74 beats/min. | The dose of norepinephrine was adjusted to 0.56ug/Kg/min, and the patient's symptoms were relieved. Vasoactive agents were continued to maintain the blood pressure at about 110/60 mmHg. |
| Admission d6(21: 30) | Blood routine, stool routine and myocardial markers were urgently examined. | The patient's condition was stable with tolerable blood pressure control.Dopamine and norepinephrine continued (dose adjusted for blood pressure). |
| Admission d7 | BP: 120-130/70-80 MMHG, heart rate 65-75 beats/min.The patient had no discomfort. | Dopamine has been discontinued, norepinephrine has been adjusted to 0.04ug/Kg/min, epinephrine has been adjusted to 0.04ug/Kg/min. |
| Admission d8 | Blood pressure: 150/90 mmHg，ECG showed:The rate of sinus rhythm was 72 beats per minute. | Forsinopril tablets 10mg bid + amlodipine besylate 5mg bid + rhythmapine 100mg tid + metoprolol succinate 23.75mg qd. |
| Admission d10 | The blood pressure and heart rate were controlled well, and the condition was basically stable. He was granted discharge. | Regular use of medications. |

## 3. Analyze and discuss

### 3.1. The interaction between old age and drugs is a high risk factor for inducing hypotension

The patient was a 74-year-old woman with a history of hypertension. Her blood pressure was generally controlled with fosinopril, amlodipine besylate, and metoprolol tartrate sustainedrelease tablets, and there was no special family history of hereditary hypertension. Propafenone hydrochloride (150mg thrice daily orally) was started on the third day of admission, and blood pressure was maintained in the normal range for the first 5 days. On the 6th day, nifedipine 20mg was added in the morning, and the blood pressure began to decrease but basically tended to normal value. At 18:00, nifedipine 20mg was given again, and the blood pressure decreased significantly, followed by hypotensive shock. Then, the clinician reviewed the relevant literature and data, and considered hypotensive shock caused by the interaction between the elderly patient and the drug. As a clinical emergency, hypotensive shock not only occurs in cases of massive hemorrhage, acute myocardial infarction, severe trauma, allergy, etc., but also caused by drug interactions. Relevant studies have reported that [3] hypotension caused by drug interactions accounts for a large proportion of clinical adverse events, especially when antihypertensive drugs and antiarrhythmic drugs are used together, as shown in Figure 1.

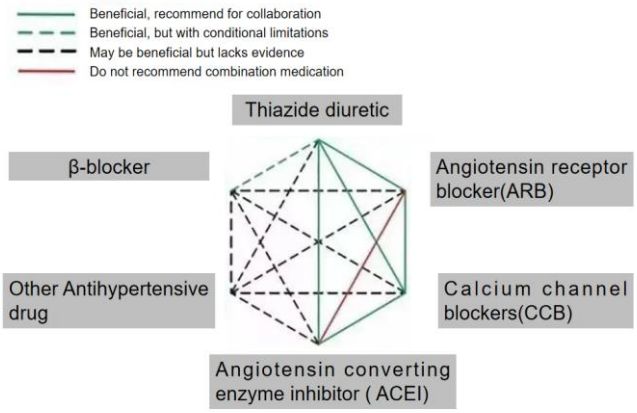


Figure 1: Combined medication rules

"Drug interactions" (DI) refers to the simultaneous use of two or more drugs to improve drug efficacy or reduce related toxic and side effects, or to reduce drug efficacy and other toxic and side effects resulting in related adverse reactions [4-5]. Therefore, the greatest adverse reaction of a combination of multiple interacting drugs is to increase or magnify the blood concentration of a drug several times, inhibit the metabolic process of the drug in the body, prolong the half-life of the drug, and thus increase the incidence of adverse events. On the other hand, old age is also a high risk factor for inducing hypotensive shock. The elderly are deficient in sensory, cognitive and expression functions and cannot clearly describe their own discomfort symptoms. Moreover, there are many underlying diseases, poor resistance and tolerance, complex medication, and higher sensitivity to some drugs may also lead to the amplification of the effect of the drug and cause some adverse reactions when the basic dosage of the drug is used. At the same time, as a special susceptible population, the elderly have many predisposing factors that cause the occurrence of coronary heart disease, valvular heart disease and hypotensive shock [6]. Based on this, the incidence of hypotensive shock will be greatly increased if the two unfavorable factors of age and drug interaction are taken into account at the same time.

### 3.2. Drug interactions between metoprolol and propafenone hydrochloride

Drug-drug interactions, as a high risk factor for inducing adverse events, were also the result of the interaction between metoprolol and propafenone hydrochloride in this case. As a β-receptor blocker [7], metoprolol has high efficiency and selectivity, which blocks and inhibits cardiac β1-receptor, reduces cardiac output, and then blocks central β-receptor. It can also inhibit the contraction level of myocardial cells, slow down the speed of myocardial contraction, and reduce myocardial oxygen consumption. At the same time, metoprolol can also resist the secretion of catecholamines in the body, increase the excitability of sympathetic nerve, reduce heart rate and inhibit myocardial contraction [8]. The instructions for the use of metoprolol recorded a 2-to 5-fold increase in the plasma concentration of metoprolol after administration of propafenone in four patients already on metoprolol. The mechanism of action is that propafenone hydrochloride also has β-receptor blocking effect, which can inhibit the concentration of metoprolol through the cytochrome P4502D6 pathway, which means that propafenone hydrochloride will increase the blood concentration of metoprolol, prolong its drug clearance half-life and enhance its heart-rate and blood-pressure lowering effect, as shown in Figure 2.

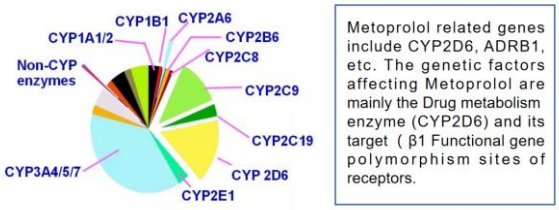


Figure 2: CYP2D6 in Cytochrome P450 single oxidase system and Metoprolol

Propafenone hydrochloride, a class IC broad-spectrum antiarrhythmic drug with sodium channel blocker, mainly acts on the conduction system of the atrium and myocardium, slowing down the conduction velocity of the myocardium, prolonging the effective refractory period, reducing the excitability of cardiomyocytes and causing systemic disorders, such as abnormal conduction of the sinus node. Atrioventricular block; Inhibition of sinus node automaticity leads to sinus bradycardia, thereby slowing the heart rate, but it also reduces cardiac output and causes hypotension [9]. Some studies have reported that propafenone hydrochloride can also dilate coronary arteries, reduce internal vascular resistance, reduce cardiac output and reduce blood pressure while treating tachyarrhythmia in the elderly [10-11]. It is also noted in the medication instructions of propafenone hydrochloride that its use with drugs metabolized by CYP2D6, metoprolol, and patients with impaired cardiac function will increase the plasma or blood levels of these drugs, thereby increasing the plasma concentration of the drug. This case also confirmed that the combination of metoprolol and propafenone hydrochloride does produce adverse reactions such as hypotension due to the interaction between the drugs in the elderly. Therefore, the heart rate and blood pressure of patients should be closely monitored during the use of metoprolol and propafenone hydrochloride to avoid the occurrence of serious adverse events such as hypotensive shock and bradycardia, so as to guide our clinicians to use drugs more reasonably.

### 3.3. Emergency treatment of hypotensive shock

When the patient became unconsciousness, diaphoretic, pale, and had a weak pulse and breathing, the clinician considered the possibility of hypotensive shock and made emergency treatment. First, the patient's vital signs (including blood pressure, temperature, pulse, and respiration) were measured immediately, and the patient was asked to increase venous blood return to the lower limbs in a supine position. At the same time, oxygen inhalation, electrocardiogram monitoring, and establishment of at

least two venous access were given. Secondly, it was given to rehydrate and replenish effective circulating blood volume, norepinephrine or dopamine was used to increase blood pressure, and atropine was used to improve heart rate. In addition, it is still necessary to appease the nervous mood of the patient's family members, stop using related drugs that may cause hypotension and adjust drug interactions, closely monitor vital signs, pay attention to keep warm, maintain body temperature, and record intake and output volume.

### 3.4. Prevention of hypotensive shock

Metoprolol and propafenone hydrochloride, as common drugs for cardiovascular diseases, have important therapeutic value for patients with arrhythmia. However, the middle-aged and elderly people and the interaction between the two drugs have also become high risk factors for the combination of metoprolol and propafenone hydrochloride, and the adverse reactions such as hypotension, nausea and vomiting also make the use of the two drugs should be cautious. Therefore, in order to avoid the clinical recurrence of the major adverse reactions caused by the combination of the two drugs, the combination of the two drugs should be avoided as far as possible. If necessary, the risk factors such as advanced age and drug interactions should be considered to adjust the drug dosage and monitor the patient's vital signs and discomfort symptoms, and symptomatic treatment should be taken at any time.

## 4. Conclusion

In summary, this paper reports a case of hypotensive shock caused by the combination of metoprolol and propafenone hydrochloride. Hypotensive shock caused by drug interactions is a clinical emergency with acute onset and severe condition, but the prognosis of patients is still very good and there are no other sequelae as long as the treatment is timely. Therefore, clarifying the interaction between drugs can also provide a reference for clinicians to use drugs in the future, so as to make them more reasonable and safe.

## References


*[1] Volpe M, Chin D, Paneni F. The challenge of polypharmacy in cardiovascular medicine [J]. Fundam Clin Pharmacol. 2010; 24(1):9-17.*

*[2] Kukreja S, Kalra G, Shah N, Shrivastava A. Polypharmacy in psychiatry: a review [J]. Mens Sana Monogr. 2013; 11(1): 82-99.*

*[3] Liao Chaofeng, Zhang Luzhao, Liu Yingzhen. To analyze the influencing factors of adverse drug events caused by potential drug interactions in elderly patients in the Department of Cardiology of our hospital [J]. Pharmacy in China, 2017, 28(14):1924-1927.*

*[4] Wang Fang, Long Xin, Zhou Gang, Liu Ningning. Drug interaction relationship extraction method based on external knowledge [J]. Journal of Sichuan University (Natural Science Edition), 2021, 58(06):55-63.*

*[5] Firkins R, Eisfeld H, Keinki C, et al. The use of complementary and alternative medicine by patients in routine care and the risk of interactions [J]. Journal of Cancer Research & Clinical Oncology, 2018, 144(3):551-557.*

*[6] Zhang Jianyu, Liang Qian, Xu Zhaoyan, Cai Weibiao, Liang Riming, Yang Xili. Characteristics of clinical manifestations and risk factors in elderly patients with chronic heart failure[J]. Application of modern drugs in China, 2020, 14(14):24-26.*

*[7] Fan Jintao, Geng Huapei, Zhao Hui, et al. Efficacy and adverse reactions of valsartan combined with metoprolol in the treatment of chronic cardiac insufficiency [J]. Hebei Medicine, 2017, 46(15): 2342-2344.*

*[8] Ding Yuming, Liu Juntian. Pharmacological characteristics and adverse reactions of metoprolol [J]. Journal of Clinical rational use of drugs, 2018, 11(10):108-110.*

*[9] Tang Sumei, Wang Shuzhen. Clinical experience of propafenone hydrochloride in the treatment of hypotension caused by paroxysmal supraventricular tachycardia [J]. Chinese and foreign medicine, 2007(23):39.*

*[10] Hu Bo. The effect of amiodarone hydrochloride on elderly patients with tachyarrhythmia [J]. Contemporary medical treatises, 2020, 18(07):110-111.*

*[11] Li Na. Clinical observation of adverse reactions of propafenone hydrochloride [J]. Modern Medicine Application in China, 2019, 13(19):106-107.*