Carvedilol In Resistant Arterial Hypertension: A Case Report

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Abstract

Background: Hypertension, a prevalent global health issue affecting approximately two-thirds of the adult population, significantly elevates the risk of cardiovascular morbidities, including ischemic heart disease, stroke, and heart failure, ultimately contributing to increased mortality rates. Resistant hypertension (RHTN), characterized by persistent blood pressure elevation despite adherence to a regimen of at least three antihypertensive agents, affects an estimated 10% of hypertensive individuals. Current clinical guidelines advocate for the addition of a fourth antihypertensive agent, such as a beta-blocker, in the management of RHTN. However, the evidence base supporting the efficacy of beta-blockers in this specific population remains limited. The PATHWAY-2 study, a key investigation in this area, demonstrated that bisoprolol, a second-generation beta-blocker, conferred a modest reduction in systolic blood pressure (8.4 mmHg). Notably, there is a paucity of data regarding the comparative effectiveness of other beta-blockers, particularly third-generation agents possessing vasodilator properties, on both systolic and diastolic blood pressure outcomes in patients with RHTN.
Aim: The addition of carvedilol, a third-generation beta-blocker with vasodilator properties, would help achieve blood pressure targets (<130/80 mmHg) in patients with RHTN.
Methods: Patients with confirmed RHTN, defined as uncontrolled blood pressure (≥140/90 mmHg) as measured by 24-hour ambulatory blood pressure monitoring. Carvedilol was added to the existing antihypertensive regimen. The primary outcome measures were changes in systolic and diastolic blood pressure following 6 weeks of carvedilol treatment.
Results: The addition of carvedilol resulted in a significant reduction in both systolic and diastolic blood pressure and achieved target blood pressure.
Conclusion: The findings of this study provide compelling evidence that carvedilol is an efficacious therapeutic option for the management of RHTN. In addition, the blood pressure reductions observed with carvedilol appear to exceed those previously reported with bisoprolol, suggesting a potential advantage for this third-generation beta-blocker in the treatment of RHTN. Further research is warranted to confirm these findings and to elucidate the underlying mechanisms responsible for the observed effects. **(TCM-GMJ June 2025; 10 (1): P15-P17)**

Keywords: Beta-blocker; carvedilol; resistant arterial hypertension.

Introduction

Hypertension remains a significant global health burden, with only 21% of patients achieving adequate blood pressure (BP) control despite widespread treatment availability[1]. Notably, approximately 30% of this population requires at least three different classes of antihypertensive medications to manage their condition[2]. Current clinical guidelines advocate for initial dual therapy, escalating to triple therapy if target blood pressure is not achieved[3]. Approximately 20-30% of hypertensive individuals exhibit resistant hypertension (RHTN), defined as failure to reach target BP (<140/90 mmHg) despite maximally tolerated doses of three antihypertensive agents, including a diuretic [4,5,6]. In such instances of resistant hypertension, where blood pressure remains above target despite a standard regimen of a renin-angiotensin-aldosterone system (RASi) inhibitor, a calcium channel blocker (CCB), and a diuretic, guidelines recommend the addition of a fourth agent. This may include spironolactone, or beta-blocker, or alpha-blocker, or centrally acting drug, or a loop diuretic (particularly in patients with chronic kidney disease and reduced creatinine clearance)[3]. However, it should be recognized that some patients exhibit intolerance to CCBs, primarily due to lower limb edema[7]. This intolerance can pose a significant challenge in achieving blood pressure control and may contribute to an increased prevalence of uncontrolled hypertension. Evi-

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dence supporting beta-blocker use in resistant hypertension is limited, primarily derived from the PATHWAY-2 trial[8]. This study demonstrated that adding bisoprolol to a regimen of RAAS blockers, CCBs, and diuretics reduced mean systolic blood pressure by 8.4 mmHg. However, significant knowledge gaps remain, including the lack of data on other beta-blockers, the absence of diastolic blood pressure reduction outcomes in PATHWAY-2. Patients with resistant hypertension had an increased risk of cardiovascular events, which supports the need for greater efforts toward improving hypertension outcomes in this population[9]. Our clinical case investigated the efficacy of carvedilol, a non-selective, third generation beta-blocker carvedilol in patients with resistant arterial hypertension.

Methods

Our patient is 69 years old male with resistant hypertension despite lifestyle modifications and optimal doses of three antihypertensive drug classes: a renin-angiotensin system inhibitor (RASi), a calcium channel blocker (CCB), and a thiazide/thiazide-like diuretic. Resistant hypertension was confirmed via 24-hour ambulatory blood pressure monitoring (ABPM), which revealed an average blood pressure of 143.4/88.2 mmHg. after patient meet inclusion criteria and did not have any exclusion criteria (see below):

Inclusion criteria:

- Age >18-75 years;
- Average systolic blood pressure by 24-hour ambulatory blood pressure monitoring (ABPM) ≥130 mmHg in case of therapeutic lifestyle interventions and pharmacotherapy with optimal doses of three different classes of blood pressure lowering agents (ACEi/ARB plus CCB plus thiazide/thiazide-like diuretic) at least for 1 month;
- Signed informed consent.
- Patients consistent with one or more of the following **criteria were excluded** from the study:
- Age <18 or >75 years;
- Severe hypertension (≥180/≥110 mmHg);
- Secondary hypertension;
- History of documented acute cardiovascular disease within six months;
- History of documented valvular heart disease;
- History of documented acute infectious disease within six months;
- History of asthma and/or severe COPD (GOLD 3 or 4);
- Clinical meaningful arrhythmias (including bradycardia) or conduction disorders;
- Congestive heart failure of III-IV NYHA functional class;
- Any contraindications of beta-blockers;
- Patients treated with carvedilol prior to enrollment in the study;
- ≥G4 categories chronic kidney disease (eGFR ≤15-29 ml/min/1.73m2);
- Decompensated chronic liver disease or >2-fold the normal upper limit (ULN) elevation of liver transaminases;
- Life-threatening co-morbidities or concurrent illnesses;
- History of alcohol/drug dependence within six months;
- Pregnancy and breastfeeding;
- Participation in another clinical trial;
- Inability to give informed consent to participate in the study.

Following confirmation, carvedilol was initiated at a dose of 12.5 mg twice daily. After one week of therapy, the patient's tolerability was assessed, and the carvedilol dose was successfully up-titrated to 25 mg twice daily.

Results and discussion

After 6 week of treatment with carvedilol on top of three antihypertensive drugs home blood pressure monitoring showed mean decrease of systolic and diastolic blood pressure 14.3 mmHg and 8.7 mmHg respectively compared to baseline blood pressure (**see figure 1 and 2**). Patient achieved target blood pressure (129.1/79.5 mmHg). This is the first clinical observational study to evaluate the efficacy of carvedilol in patients with resistant hypertension. Carvedilol is a third-generation non-cardioselective vasodilator β-blocker. Compared with conventional β-blockers, carvedilol maintains cardiac output, has a reduced prolonged effect on heart rate, and reduces blood pressure by decreasing vascular resistance[10]. Carvedilol blocks norepinephrine binding to α1-adrenergic receptors in addition to both β1-adrenergic and β2-adrenergic receptors[11,12,13]. This results in a reduction in arterial BP by maintaining cardiac output and decreasing total β-adrenoreceptor vasoconstrictor tone[14,15]. In contrast to the PATHWAY-2 study, which focused solely on bisoprolol and its impact on systolic blood pressure alone, our study encompassed not only systolic, but diastolic blood pressure assessments. In PATHWAY-2 study bisoprolol did lower blood pressure (-8.4 mmHg) compared to placebo (-3.4 mmHg), but the reduction was smaller than that observed with spironolactone[8]. Specifically, spironolactone reduced home systolic blood pressure by 6.48 mmHg more than bisoprolol[10]. Unlike the PATHWAY-2 study, which relied on home blood pressure measurements, our study utilized 24-hour ambulatory blood pressure monitoring to collect the first data and conformation of resistance of hypertension.

Conclusion

In conclusion, our study has shown that carvedilol is effective in patients with resistant. Furthermore, it is important to note its advantage over the effect of bisoprolol (seen in the PATHWAY 2 study). Carvedilol showed a clinically significant reduction in blood pressure represented in our case. Future research using a larger randomized controlled design is needed to definitively assess the comparative efficacy of carvedilol versus individual beta-blockers in reducing blood pressure.

Figure 1, Effect of Carvedilol on systolic blood pressure reduction, after 6 weeks of treatment

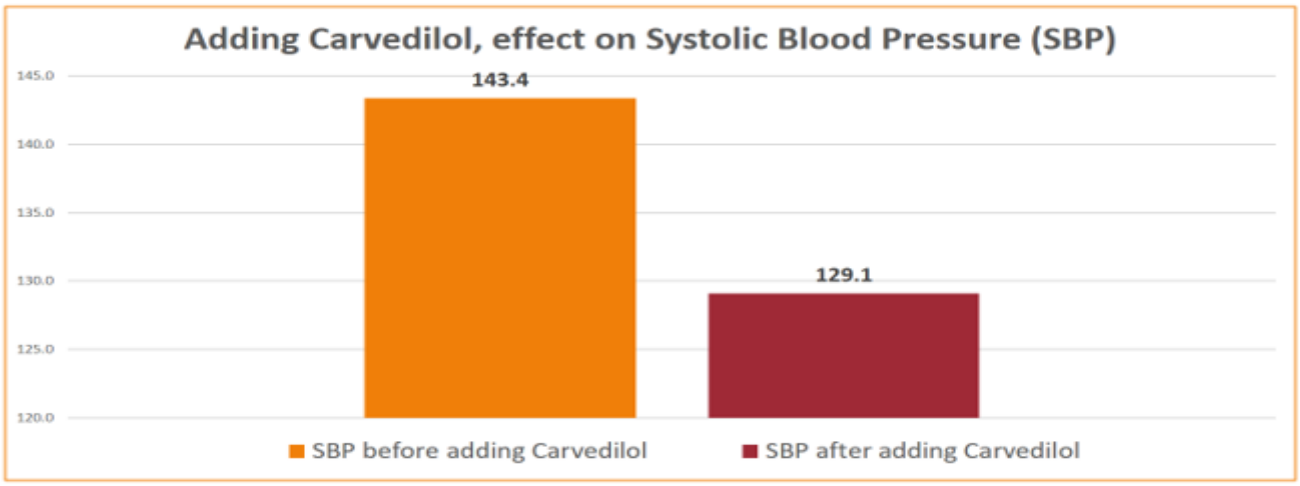
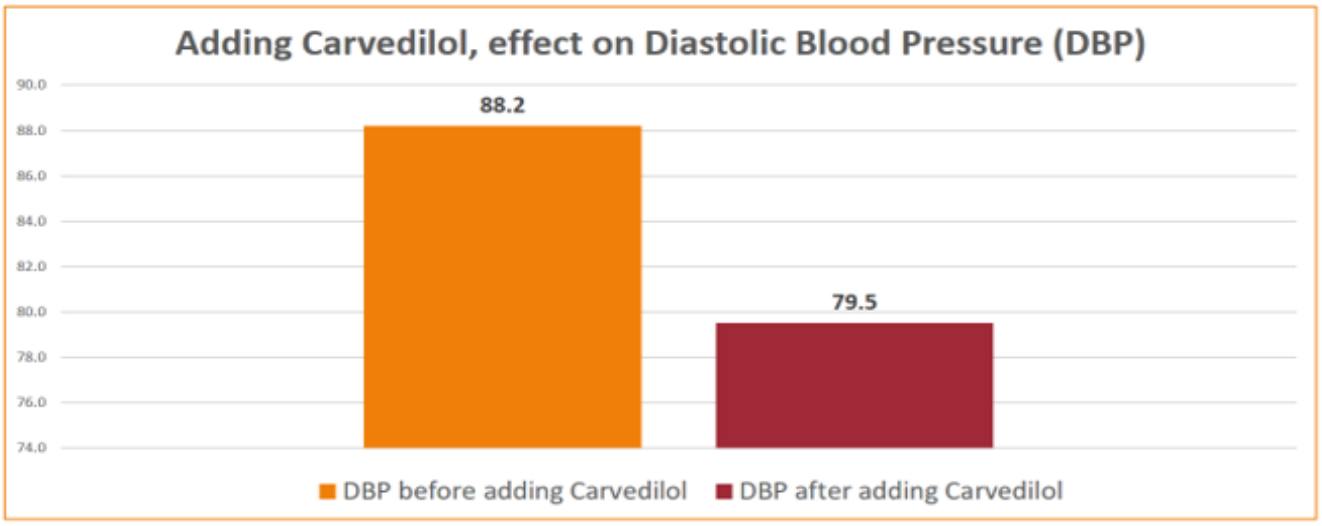


Figure 2, Effect of Carvedilol on diastolic blood pressure reduction after 6 weeks of treatment



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