Update in Hypertension Therapy

by Peter J. Lin, MD, CCFP

INTRODUCTION

Hypertension is a significant risk factor for cerebrovascular disease, coronary artery disease (CAD), congestive heart failure, renal failure, peripheral vascular disease (PVD), dementia and atrial fibrillation.[1] The goal of therapy is to reduce the blood pressure (BP) to below recommended thresholds (below 140/90 mmHg for most patients and below 130/80 mmHg for those with diabetes).[2]

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Achieving BP control often requires a multifaceted approach—the 2008 recommendations of the Canadian Hypertension Education Program (CHEP) state that control of BP usually requires two or more antihypertensive drugs in addition to lifestyle modifications.[2]

The observation that two or more drugs are usually required is an important one. Clinicians need to be aware of the likelihood of needing to use antihypertensive combinations and become familiar with combinations that work well together. Of note, the 2008 CHEP recommendations also state that using fixed-dose combination pills (rather than prescribing two agents in two separate pills) may be an effective way to optimize adherence.

The following case vignettes provide illustrations of scenarios where fixed-dose combination antihypertensive therapy would be an appropriate choice.

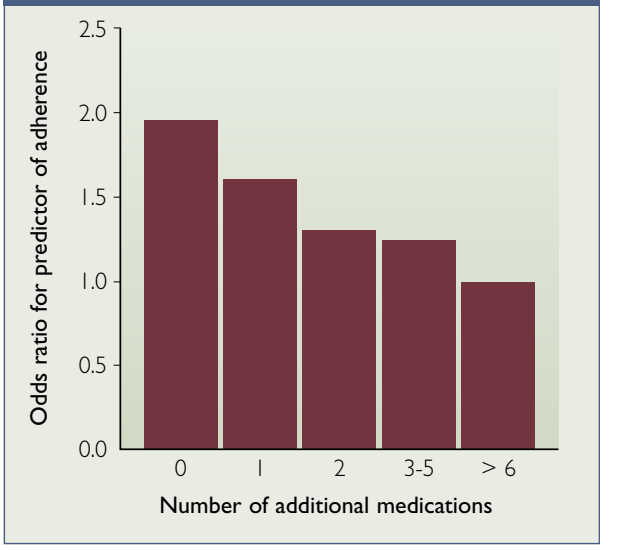
CASE STUDY 1: MR. LP

Mr. LP is a 62-year-old postal worker with a 14-year history of hypertension, a 12-year history of type 2 diabetes and dyslipidemia, and a 40-year history of cigarette smoking. He presents to the office to renew his prescriptions. His BP is found to be controlled, at 128/76 mmHg.

He is currently taking eight medications:

- amlodipine 10 mg OD;
- atorvastatin 40 mg OD;
- ramipril 10 mg OD;
- hydrochlorothiazide (HCTZ) 25 mg OD;
- metformin 500 mg BID;
- rosiglitazone 2 mg BID;
- glyburide 10 mg BID; and
- enteric-coated acetylsalicylic acid (ECASA) 81 mg OD.

FIGURE 1 Impact of Dosing Regimen on Medication Adherence



With the number of medications Mr. LP is taking, the physician is concerned about adherence. Several studies have demonstrated that there is an inverse correlation between daily dose frequency and the rate of medication adherence (Figure 1).

The physician therefore recommends substituting fixed-dose combination pills for some of his individual medications. The combination of ramipril 10 mg and HCTZ 25 mg, for example, is available in one tablet (Altace® HCT); amlodipine and atorvastatin are also available together in one pill (Caduet®), as are metformin and rosiglitazone (Avandamet®). By making these three substitutions in Mr. LP's regimen, the likelihood of adherence is improved and the overall cost of therapy is reduced.

CASE STUDY 2: MR. HR

Mr. HR is a 58-year-old stock broker, who presents to the office for a regular follow-up. He has a five-year history of type 2 diabetes and dyslipidemia. His current medication regimen includes:

- ECASA 81 mg OD;
- atorvastatin 10 mg OD; and
- metformin 500 mg BID;
- ramipril 10 mg OD.

His BP is found to be uncontrolled, at 146/90 mmHg (patients with diabetes should be controlled to below 130/80 mmHg).[3]

In an effort to control Mr. HR's BP, the physician elects to add another antihypertensive to the pharmacologic regimen. Since Mr. HR is already receiving an angiotensin converting enzyme (ACE) inhibitor, his physician opts to add a fixed dose combination which would keep the pill count the same and improve compliance while improving control of hypertension.

Another strategy for combination therapy in this case might be the addition of a calcium channel blocker (CCB) to the ACE inhibitor (*i.e.*, based on the results of the Avoiding Cardiovascular Events Through Combination Therapy in Patients Living with Systolic Hypertension [ACCOMPLISH] study).[4] However, at this time the CHEP recommendations do not advocate the use of any particular combination over another. It is anticipated that this study's results, once published, will be reflected in the CHEP recommendations regarding which combinations might be of greatest benefit.

CASE STUDY 3: MR. VP

Mr. VP is a 55-year-old truck driver with an eight-year history of type 2 diabetes and hypertension. He is currently receiving HCTZ 25 mg OD and metformin 500 mg BID.

Mr. VP's hypertension is currently 140/90 mmHg. In light of the results of the HOPE study,[5] and the recommendation from the Canadian Diabetes Association to prevent macrovascular complications, his physician considers whether or not he is a candidate for vascular protective therapy with ramipril. In the Heart Outcomes Prevention Evaluation (HOPE) study, ramipril 10 mg was found to reduce the combined incidence of CV death, MI and stroke by 22% when added to existing therapy.

TABLE 1 Inclusion Criteria for the HOPE Study

- Men and women ≥ 55 years old
- History of CAD, stroke or PVD, or diabetes plus at least one other cardiovascular risk factor:
  - Hypertension
  - Elevated total cholesterol levels
  - Low high-density lipoprotein (HDL) cholesterol levels
  - Cigarette smoking
  - Documented microalbuminuria

Looking at the inclusion criteria for the HOPE study (Table 1), Mr. VP would indeed have been eligible for the trial based on his age, diabetes and hypertension.

As such, the physician elects to add ramipril 10 mg to Mr. VP's medication regimen. He can do so without increasing the pill burden or cost by replacing the HCTZ 25 mg with a fixed-dose combination of ramipril 10 mg and HCTZ 25 mg. Based on the recently published ONTARGET[7] results, it appears an ARB would also be a suitable option. When adding an ACE inhibitor or an ARB in a patient already taking a diuretic, care should be taken to avoid dehydration which could cause creatinine levels to rise.

CASE STUDY 4: MRS. MI

Mrs. MI is a 62-year-old school teacher. Three months ago, she suffered an acute MI. Two months later, she underwent a percutaneous coronary intervention with bare metal stent insertion. Her current medication regimen includes:

- metoprolol 50 mg BID;
- atorvastatin 80 mg OD;
- ramipril 10 mg OD;
- ECASA 81 mg OD; and clopidogrel 75 mg OD.

Her BP is currently 140/95 mmHg. This is above the 140/90 mmHg threshold established by the CHEP. Also, given that she is such a high-risk patient, one might also consider aiming for a considerably lower target BP—130/80 mmHg or lower.

Because she is already on ramipril, the physician elects to add a diuretic, HCTZ to the regimen. This can be accomplished through the substitution of the ramipril/HCTZ fixed-dose combination for her existing ramipril tablet. Although some might consider adding an angiotensin receptor blocker (ARB), given that they have also been found to provide vascular protection in the post-MI setting, combined ACE-inhibitor and ARB therapy has not been shown to provide additional protective efficacy and may be associated with undesirable adverse events.[6] Therefore, adding a diuretic—or perhaps a CCB in cases of distant MI—might be most appropriate in this case.

CASE STUDY 5: MS. ON

Ms. ON is a 66-year-old woman recently retired from her position as an administrative assistant. She has a 10-year history of type 2 diabetes and has been treated with ramipril 10 mg OD for the past eight years. At the time of presentation, her BP was 140/90 mmHg.

At this point, according to CHEP, her BP is uncontrolled (target BP for a person with diabetes is less than 130/80 mmHg). An additional antihypertensive should be added. Given that the CHEP guidelines recommend either an ACE-inhibitor or an ARB as primary antihypertensive therapy for patients with diabetes, the physician considers whether or not it is advisable to add an ARB to this regimen.

The ONTARGET trial is informative for this situation.[7] In that study, ramipril was compared to telmisartan or the combination of the two drugs in patients with vascular disease or high-risk diabetes. The primary composite efficacy outcome was death from cardiovascular causes, MI, stroke, or hospitalization for heart failure. The investigators reported that the combination of the two drugs was associated with more adverse events without an increase in benefit. There was no significant difference between the two monotherapies.

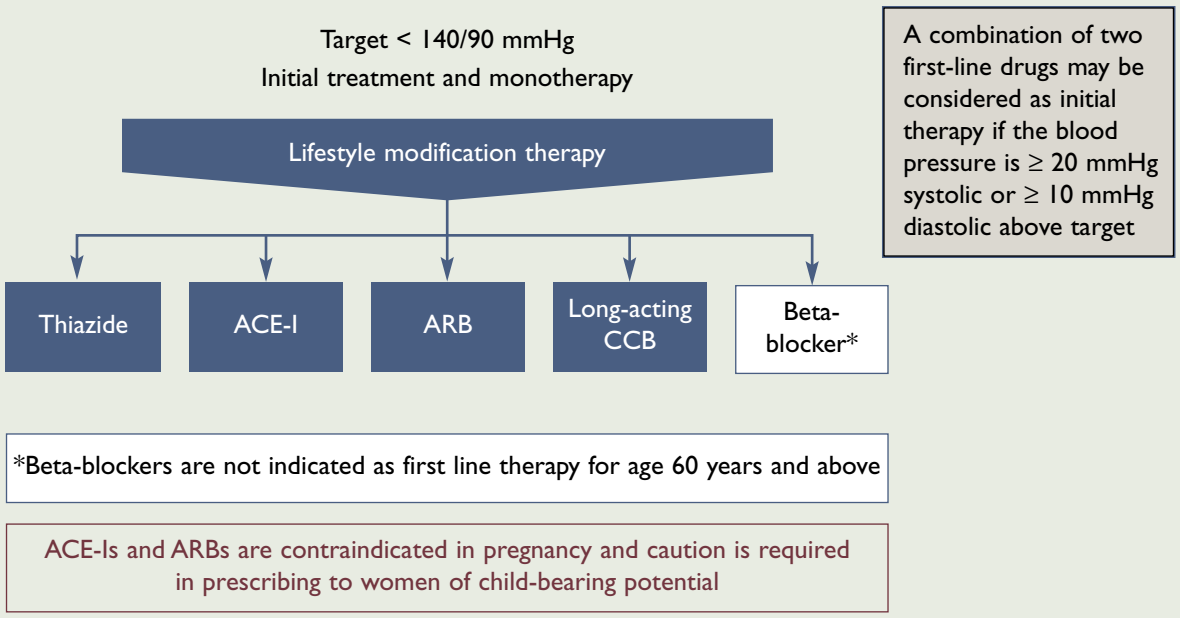
Therefore, the physician elects to switch Ms. ON from her ramipril monotherapy to a fixed-dose combination of ramipril and HCTZ. Adding a CCB may also be considered, particularly given the findings of the ACCOMPLISH study.[4]

CASE STUDY 6: MR. BP

Mr. BP is a 57-year-old software programmer. On routine investigation, he was found to have an elevated BP (168/100 mmHg on multiple readings). There is no evidence of end-organ damage, nor have any secondary causes of hypertension been identified. He is not suffering from any acute chest pain or headaches (which would constitute hypertensive emergencies).

The current BP is markedly elevated and requires immediate pharmacologic treatment. Furthermore, according to the CHEP recommendations, when the systolic BP is more than 20 mmHg from target or if diastolic BP is more than 10 mmHg from target (both are true in this case) initial combination therapy may be considered (Figure 2).[2]

FIGURE 2 Treatment of Adults with Systolic/Diastolic Hypertension without Other Compelling Indications (2008 CHEP Recommendations)



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