FIMS Position Statement

Antihypertensive medications and exercise

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Introduction

Over recent decades, lifestyles have undergone substantial changes. A combination of increased fat and refined carbohydrates in the diet, and a reduction in physical activity has resulted in an epidemic of hypertension, obesity, type 2 diabetes mellitus, and other chronic diseases. Adoption of healthy lifestyles by all individuals is critical for the prevention of high blood pressure (BP). Furthermore, according to The Seventh Report of the Joint National Committee on Prevention, Evaluation, and Treatment of High Blood Pressure, adoption of a healthy lifestyle forms an indispensable part of the management of patients with hypertension. In fact, positive lifestyle modifications, including physical exercise training, may have similar efficacy to single drug therapy. Lifestyle changes, however, should not delay unnecessarily the initiation of pharmacotherapy, especially in patients with higher risk of cardiovascular disease. Thus many patients should receive an exercise prescription, in addition to an antihypertensive medication prescription from the treating clinician.

Some antihypertensive agents interfere with the normal physiological response to exercise leading to fatigue and making exercise an unpleasant experience as perceived by the patient. This often results in non-compliance with the exercise prescription or the pharmacological prescription, or both.

Antihypertensive medications and their effect on exercise physiology

A list of the categories of antihypertensive agents including examples of individual and combination agents is presented in Table 1. The effects of these groups of agents are briefly reviewed:

1. Beta-blockers

These agents lower heart rate-pressure product and cardiac output, alter fuel utilisation, thermoregulation, skeletal muscle recruitment patterns, and increase ratings of perceived exertion during prolonged submaximal exercise. Although exercise tolerance in athletes and certain non-ischaemic patients might be reduced, in patients with myocardial ischaemia these agents may increase exercise tolerance. The effects of these agents on exercise are detrimental to competition; however, the benefits of chronic exercise training are nonetheless achieved. In general, beta-blockers are not the most efficacious class of antihypertensives.
2. **Diuretics**

These agents generally do not alter the haemodynamic response to exercise but can lower exercise blood pressure in some hypertensive patients\(^9\). Exercise tolerance is generally not adversely affected and can in fact be enhanced if the patient has congestive heart failure. Use of these agents can cause premature ventricular contractions (PVCs) or false positive ECGs, particularly if hyopkalaemia results from their use. Whilst these agents are generally cost effective and thus used worldwide, they may predispose the patient to mild-moderate dehydration or hypokalaemia which is undesirable for those participating in prolonged exercise in the heat.\(^{20,21}\)

3. **Nitrates**

These agents might increase heart rate and lower blood pressure at rest and during exercise and might improve exercise tolerance in patients with myocardial ischaemia and/or congestive heart failure. Exercise tolerance might be affected in certain non-ischaemic hypertensive patients by vasodilatation and near syncope.\(^9\)

4. **Calcium Channel Blockers**

These agents have a variable effect on resting and exercise heart rate and generally lower the blood pressure response during exercise. These agents usually increase exercise tolerance in patients with myocardial ischaemia. Exercise tolerance in non-ischaemic hypertensive patients is mostly unaffected, making these agents a good choice for athletes.\(^{9,12,22-24}\)

5. **Angiotensin-Converting Enzyme (ACE) inhibitors and Angiotensin II Receptor Blockers**

These agents generally do not alter the heart rate response or exercise tolerance during submaximal exercise, yet the blood pressure response is typically reduced. Therefore ACE inhibitors are a good choice for hypertensive athletes. Exercise tolerance in patients with heart failure might be improved through use of these agents.\(^{25-27}\)

6. **Older antihypertensive agents, including vasodilators and centrally acting agents**

Whilst these agents have been used in athletic populations in the past, most agents in this group are ingested twice to three times a day and therefore multiple doses are a disadvantage. Furthermore patients have reported cardiac awareness, light-headedness on exertion and tachycardia, which has resulted in decreased use of these agents in the physically active hypertensive population.

7. **Combination agents**

Effects of these agents are generally as per the individual components. Hydrochlorothiazide can enhance the effects of other antihypertensive agents. Therefore hypertensive athletes can use lower doses of two medications to get the same efficacy of much higher doses of single agents.

**Practical recommendations for use of antihypertensive agents in exercising individuals**

Prescription of antihypertensive medications for active individuals should be individualised and based on the efficacy of the agent, response of the individual to the agent and the effects on exercise tolerance.

As beta-blockers may have considerable negative effects on exercise tolerance in certain patients, clinicians should be vigilant for these adverse effects and if present should prescribe alternative antihypertensive agents. ACE inhibitors, angiotensin II receptor blockers and calcium channel blockers are generally preferred in physically active hypertensive
individuals as they do not alter exercise tolerance to the same extent as the beta blockers.

If the prescribing clinician wishes to use a beta blocking agent (e.g. in hypertensive patients with ischaemia), beta1 selective blockers should be prescribed rather than non-selective beta blockers.

Use of beta-blocking agents will alter heart rate-based exercise prescription, thus patients ingesting these agents should undergo exercise testing whilst using the agents. Heart rate-based prescription should be adjusted accordingly.

Non-selective beta-blocking agents might increase predisposition to hyperthermia and hypoglycaemia during exercise. Therefore patients using these agents, who participate in prolonged exercise in the heat, should be encouraged to adhere to accepted guidelines for the prevention of heat injury and methods to prevent hypoglycaemia.

Vasodilators, calcium channel blockers and alpha-blockers may cause hypotensive episodes on rapid cessation of exercise. A longer cool-down period is therefore recommended.

As blood pressure in hypertensive individuals tends to be attenuated by exercise training, hypotension at rest or during the exercise bout could become clinically significant over time. The clinician should be aware of this trend and adjust the dose of the antihypertensive agent accordingly.

Anti-doping considerations

It is important to note that both beta-blockers (certain sports) are diuretics (all sports) are prohibited agents according to the World Anti Doping Agency (WADA) code. Therefore physicians should exercise caution when prescribing these agents to competitive hypertensive patients. Therapeutic Use Exemption (TUE) would be required prior to initiation of therapy.

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References

8. Derman WE, Sims R, Noakes TD. The effects of antihypertensive medications on the physiological response to maximal exercise testing.
Antihypertensive medications and exercise


Table 1: List of generic antihypertensive agents

1. **β-Blockers**
   - Acebutolol**
   - Atenolol
   - Betaxolol
   - Bisoprolol
   - Esmolol
   - Metoprolol
   - Nadolol
   - Nebivolol
   - Penbutolol**
   - Pindolol**
   - Propranolol
   - Sotalol
   - Timolol

**Beta-Blockers with intrinsic sympathomimetic activity.

2. **Diuretics**
   (a) **Thiazides**
   - Chlorothiazide
   - Hydrochlorothiazide (HCTZ)
   - Polythiazide
   - Indapamide
   - Metolazone
   (b) **“Loop” Diuretics**
   - Bumetanide
   - Ethacrynic Acid
   - Furosemide
   - Torsemide
   (c) **Potassium-Sparing Diuretics**
   - Amiloride
   - Triamterene
   (d) **Aldosterone Receptor Blockers**
   - Eplerenone
   - Spironolactone

3. **Nitrates**
   - Amyl nitrite
   - Isosorbide mononitrate
   - Isosorbide dinitrate
   - Nitroglycerin, sublingual
   - Nitroglycerin, translingual
   - Nitroglycerin, transmucosal
   - Nitroglycerin, sustained release
   - Nitroglycerin, transdermal
   - Nitroglycerin, topical

4. **Calcium Channel Blockers (Nondihydropyridines)**
   - Diltiazem Extended Release
   - Verapamil Immediate Release
   - Verapamil Long Acting
   - Verapamil – Coer
Calcium Channel Blockers (Dihydropyridines)
- Amlodipine
- Felodipine
- Isradipine
- Nicardipine Sustained Release
- Nifedipine Long-Acting
- Nimodipine
- Nisoldipine

5. Angiotensin-Converting Enzyme (ACE) Inhibitors
- Benazepril
- Captopril
- Cilazapril
- Enalapril
- Fosinopril
- Lisinopril
- Moexipril
- Perindopril
- Quinapril
- Ramipril
- Trandolapril

6. Angiotensin II Receptor Blockers
- Candesartan
- Eprosartan
- Irbesartan
- Losartan
- Olmesartan
- Telmisartan
- Valsartan

7. Other older antihypertensive agents including vasodilators and centrally acting agents
   (a) α- and β-Adrenergic Blocking Agents
       - Carvedilol
       - Labetalol
   (b) Direct Peripheral Vasodilators
       - Hydralazine
       - Minoxidil
   (c) α1 – Adrenergic Blocking Agents
       - Doxazosin
       - Prazosin
       - Terazosin
   (d) Central α2 – Agonists and other Centrally Acting Drugs
       - Clonidine
       - Guanfacine
       - Methyldopa
       - Reserpine
8. Combination antihypertensive agents

(a) β-Blockers in Combination with Diuretics
- Atenolol + chlothalidone
- Bisoprolol + hydrochlorothiazide
- Propranolol LA + hydrochlorothiazide
- Metoprolol + hydrochlorothiazide
- Nadolol + bendroflumethiazide
- Timolol + hydrochlorothiazide

(b) Central α2 – Agonists in Combination with Diuretics
- Methyldopa + hydrochlorothiazide
- Reserpine + hydrochlorothiazide
- Reserpine + chlothalidone

(c) ACE Inhibitors in Combination with Diuretics
- Benazepril + hydrochlorothiazide
- Captopril + hydrochlorothiazide
- Enalapril + hydrochlorothiazide
- Lisinopril + hydrochlorothiazide
- Moexipril + hydrochlorothiazide
- Quinapril + hydrochlorothiazide

(d) ACE Inhibitors in Combination with Calcium Channel Blockers
- Benazepril + Amlodipine
- Enalapril + felodipine
- Trandolapril + verapamil

(e) Angiotensin II Receptor Antagonists in Combination with Diuretics
- Candesartan + hydrochlorothiazide
- Eprosartan + hydrochlorothiazide
- Irbesartan + hydrochlorothiazide
- Losartan + hydrochlorothiazide
- Telmisartan + hydrochlorothiazide
- Valsartan + hydrochlorothiazide

(f) Diuretic Combination with Diuretic
- Triameterene + hydrochlorothiazide
- Amiloride + hydrochlorothiazide

Adapted from: ACSM’s Guidelines for Exercise Testing and Prescription. 7th ed. 2006, Appendix A. This is not an exhaustive list of antihypertensive medications.