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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 [1]. 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 [2]. In fact, positive lifestyle modifications, including physical exercise training, may have similar efficacy to single drug therapy[3;4]. 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[5 6].

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 [7-9]. 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 [10-15]. Although exercise tolerance in athletes and certain non-ischaemic patients might be reduced, in patients with myocardial ischaemia these agents may increase exercise tolerance[16;17]. The effects of these agents on exercise are detrimental to competition; however, the benefits of chronic exercise training are nonetheless achieved[18]. In general, beta-blockers are not the most efficacious class of antihypertensives.

International SportMed Journal, Vol.9 No.1, 2008, pp.32-38, http://www.ismj.com

2. Diuretics

These agents generally do not alter the haemodynamic response to exercise but can lower exercise blood pressure in some hypertensive patients[19]. 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

International SportMed Journal, Vol.9 No.1, 2008, pp.32-38, http://www.ismj.com

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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International SportMed Journal, Vol.9 No.1, 2008, pp.32-38, http://www.ismj.com

Table 1: List of generic antihypertensive agents

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

**Beta-Blockers with intrinsic sympathomimetic activity.

International SportMed Journal, Vol.9 No.1, 2008, pp.32-38, http://www.ismj.com

Calcium Channel Blockers (Dihydropryridines)

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

International SportMed Journal, Vol.9 No.1, 2008, pp.32-38, http://www.ismj.com

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 + chlothalidone
	Reserpine + hydrochlorothiazide
(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.