

Advantages and Disadvantages of Beta-Adrenergic Blocking Drugs in Hypertension

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General Measures

Elevation of blood pressure should be regarded as one of a number of potential risk factors for cardiovascular disease—albeit a major risk factor—rather than a disease per se.¹ It is important to identify additional risk factors in the hypertensive patient, not only because collectively these factors may greatly magnify the cardiovascular risk, but also because modification of them may, of itself, lower the blood pressure and thus alleviate the risk and save the patient the inconvenience, expense, and potential harm that may result from even the simplest of drug regimes.

Careful consideration should be given to the patient's diet (particularly in relation to the calorie intake in the case of obesity, the cholesterol and saturated fat content in the case of hyperlipidemia and patients at high risk, and the salt content) and to smoking habits, physical activity, stress, personality, and drug therapy, especially anovulant preparations. Other diseases, such as diabetes mellitus, which are associated with a high incidence of hypertension and primary causes of hypertension must be excluded. Although there is still no statistical evidence to show that modification of these risk factors—with the exception of tobacco and anovulant preparations—will actually reduce mortality, it does seem prudent on the basis of the evidence available to encourage the hypertensive patient to adjust his or her life-style not only to reduce the cardiovascular risk,² but also because in many instances the mildly hypertensive patient will respond to this approach alone.

Drug Policy

Thiazide Diuretics. Drug treatment of hypertension should begin with a thiazide diuretic, except in severe cases and in patients with overt diabetes or gout. This treatment alone may be effective in reducing blood pressure.³ Further-

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more, thiazide diuretics potentiate most other antihypertensive drugs, including beta-adrenergic blocking agents.⁴ Side effects include diabetes mellitus, the risk of which is difficult to assess but is probably not very high⁵; hyperuricemia, which is fairly common; gout, which is rare⁶, and hypokalemia, which is not a major problem (potassium supplementation is probably not necessary in hypertension).⁷

Beta-Adrenergic Blocking Drugs. It is now well established that this group of drugs is effective in treating patients with all grades of hypertension,^{8,9} and because these drugs are potentiated by thiazide diuretics, it is general policy to use this combination in most patients with hypertension.^{3,4}

Vasodilator Drugs. Vasodilators alone are not effective antihypertensive drugs because the reduction in arterial pressure due to vasodilation results in reflex baroreceptor stimulation with increased adrenergic activity, which in turn reduces or abolishes completely the hypotensive effect. However, if prior beta blockade is achieved by the administration of beta-adrenergic blocking drugs, this reflex autonomic activity is prevented and vasodilators may then have a significant hypotensive action.

In patients with resistant or severe hypertension, the combination of a thiazide diuretic, a beta-adrenergic blocking drug, and a vasodilator will usually prove effective. Hydralazine, when combined with a beta-blocker is most effective.¹⁰ Side effects, including headache, palpitations, and flushing, are considerably reduced by prior beta-blockade. Hydralazine-induced disseminated lupus erythematosus is probably dose-related and therefore unlikely to occur at the dose levels used in hypertension, but because of the likely chronicity of therapy, this side effect, which is reversible on withdrawal of the drug, should be watched for in all patients in treatment.

Advantages of Beta-Adrenergic Blockers

Comparative Freedom from Side Effects. Although the beta-blockers have many individual side effects, when compared to many other antihypertensive drugs, they are remarkably free of a number of troublesome side effects that have bedeviled the treatment of hypertension for many years. The drowsiness, lethargy, and nasal congestion so common with methyldopa,¹¹ the interference with sexual function and postural hypotension frequently encountered with the adrenergic neurone blocking drugs,¹² and the serious withdrawal phenomena found with clonidine¹³ are not frequent manifestations of beta-blocker therapy.

Once-Daily Treatment. Almost one-third of the patients on antihypertensive treatment fail to take exactly the prescribed dosage,¹⁴ and perhaps two-fifths of these patients have inadequately controlled blood pressure.¹⁵ It is perhaps understandable that the asymptomatic hypertensive patient finds it difficult to adhere to a drug regimen necessitating the ingestion of tablets four, three, or even two times daily indefinitely. Patient cooperation in therapy would prob-

ably be considerably improved by once-daily dosage of antihypertensive drugs, which might be presented in a monthly pack. Thiazide diuretics may be administered on a once-daily basis, and there is now good evidence that most, if not all, beta-adrenergic blocking drugs may be administered once daily for the treatment of hypertension.^{16,17} This property of the beta-blockers may prove to be a major advance in the management of hypertension. A further advantage of the beta-blockers is the presence of bradycardia as an indicator of patient compliance.

Treatment of Associated Conditions. Angina pectoris, cardiac arrhythmias, and an anxiety state are not uncommonly associated with hypertension, and each will respond to treatment with beta-adrenergic blocking drugs and thus minimize the treatment regimen. Furthermore, there is now some evidence that beta-blockers may protect individuals at risk from cardiovascular disease (notably coronary heart disease) from the adverse effects of sympathetic overactivity, but it would still be premature to advocate the widespread use of these drugs for their cardioprotective effect.¹⁸ However, beta-blockers may prove most useful in hypertensive patients with anxiety or patients whose personality response to stress is undesirable.

Disadvantages of Beta-Adrenergic Blocker

Predictable Adverse Reactions. There are a number of predictable pharmacologic actions of beta-blockers: bradycardia, heart block, cardiac failure, bronchospasm, cold extremities, claudication, Raynaud's phenomenon, diarrhea, fatigue, muscle cramps, weakness, dizziness, hallucinations, vivid dreams, and sleep disturbance. There is considerable individual variation in these effects, and careful patient selection will ensure that they do not occur too often. In clinical practice the benefit of cardioselectivity is small, and the cardioselective action should not be misinterpreted as a cardiospecific effect.¹⁹

Unpredictable Adverse Reaction. Nausea, anorexia, vomiting, fatigue, lassitude, ataxia, anxiety, confusion, hallucinations, insomnia, vivid dreams, the masking of hypoglycemia in patients on antidiabetic treatment, and a paradoxical hypertensive response may occur, but these effects are often dose-related and unlikely to occur at moderate dose levels.

Withdrawal Effects. Sudden withdrawal of beta-blockers may result in cardiac arrhythmias or an exacerbation of symptoms of ischemic heart disease, sometimes with the occurrence of myocardial infarction,²⁰ but the cardiovascular effects of beta-blocker withdrawal are not as striking as those of some other antihypertensive drugs.²¹ However it would seem unwise suddenly to withdraw these drugs, especially when the dosage has been high or the treatment prolonged.⁴

Relative Contraindications. Chronic obstructive lung disease, severe cardiomegaly, mild cardiac failure, pregnancy, allergic rhinitis, diabetes mellitus, and

sinus bradycardia have all been cited by manufacturers as relative contraindications, but each case must be judged on its own merits.³

Practolol-like Side Effects. It is unlikely that the oculomucocutaneous syndrome associated with practolol will occur with other beta-adrenergic blocking drugs, but considerable vigilance is necessary on the part of the medical profession, particularly in view of the somewhat indiscriminate marketing of many new beta-blockers.

Expense. The beta-adrenergic blocking drugs are expensive in comparison with many other antihypertensive preparations, but this expense must be evaluated in light of both the efficacy of treatment and the quality of life of the patient. It is now widely accepted that beta-adrenergic blocking drugs, either alone or in combination with other antihypertensive drugs, effectively control hypertension with few or no adverse reactions, and the facility of once-daily dosage may greatly enhance patient adherence to therapy.

Summary

This paper reviews the role of beta-adrenergic blocking drugs in the treatment of hypertension. A significant proportion of patients presenting with mild or moderate hypertension will respond to general measures and do not require specific drug therapy. Of the remaining patients, some will respond to treatment with a thiazide diuretic alone, and those with severe grades of hypertension will require the addition of a beta-adrenergic blocking drug, occasionally together with a vasodilator. The advantages of beta-adrenergic blocking drugs alone or in combination and the problems associated with therapy are discussed.

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