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Review

The Evolving Role of β-Adrenergic Receptor Blockers in Managing Hypertension

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ABSTRACT

β-Adrenergic blocking agents (or β-blockers) have been widely used for the treatment of hypertension for the past 50 years, and continue to be recommended as a mainstay of therapy in many national guidelines. They have also been used in a variety of cardiovascular conditions commonly complicating hypertension, including angina pectoris, myocardial infarction (MI), acute and chronic heart failure, as well as conditions like essential tremor and migraine. Moreover, they have played a primary role in controlling blood pressure in patients with these specific comorbidities and in reducing cardiovascular risk with regard to the composite outcome of death, stroke, and MI among patients younger than 60 years of age. However, in patients 60 years of age or older, β-blockers were not associated with significantly lower rates of MI, heart failure or death, and demonstrated higher rates of stroke compared with other first-line therapies. Consequently, the Canadian Hypertension Education Program recommends the use of β-blockers as first-line therapy in hypertensive patients younger than 60 years of age but not for those age 60 and older, with the exception of patients with concomitant β-blocker-requiring cardiac diseases. Several reports suggest that the lack of consistent outcome data may relate to the use of traditional β-blockers such as atenolol and their ability only to reduce cardiac output, without beneficial effect on peripheral vascular resistance. The present report will describe the clinically relevant mechanisms of action of β-blockers, their pharmacological differences, their metabolic effects, and their usefulness in patients with hypertension.

RÉSUMÉ

Les inhibiteurs de récepteurs β-adrénergiques (β-bloquants) ont été largement utilisés pour le traitement de l'hypertension artérielle au cours des 50 dernières années, et ils continuent d'être recommandés comme une thérapie principale dans de nombreuses directives nationales. Ils sont aussi utilisés dans le traitement de nombreuses pathologies cardiovasculaires notamment l'angine, l'infarctus du myocarde et l'insuffisance cardiaque. Conséquemment, ils continuent de jouer un rôle de premier plan dans le contrôle de la pression artérielle particulièrement chez les patients atteints de problèmes cardiovasculaires concomitants. Globalement, ils ont démontré une diminution du risque cardiovasculaire combiné (mortalité, AVC, infarctus du myocarde) chez les patients de moins de 60 ans. Cependant, chez ceux âgés de plus de 60 ans, les β-bloquants n'ont pas permis de réduire l'incidence combinée de mortalité, d'infarctus du myocarde et d'insuffisance cardiaque. Ils ont de plus été associés à une augmentation de la survenue des AVC, lorsque comparés aux autres classes d'agents antihypertenseurs. Le Programme Éducatif Canadien sur l'Hypertension recommande de privilégier aux patients de moins de 60 ans l'usage des β-bloquants comme traitement de première intention, à moins que ceux-ci présentent une maladie cardiovasculaire concomitante. Plusieurs auteurs suggèrent que les données probantes en défaveur de cette classe d'agents pourraient être reliées à l'utilisation de β-bloquants plus traditionnels comme l'aténolol et ce, en raison de leurs effets principalement en lien avec la réduction du débit cardiaque, sans effet significatif sur la résistance vasculaire périphérique. Cet article vise donc à décrire le mécanisme d'action des β-bloquants, leurs caractéristiques pharmacologiques, leurs effets métaboliques ainsi que leur utilité clinique chez les patients atteints d'hypertension artérielle.

β-Adrenergic blocking agents (β-blockers) have been widely used for the treatment of hypertension for the past 50 years and continue to be recommended as a mainstay of therapy in many national guidelines.[1,2] They have also been used in a variety of cardiovascular conditions including angina pectoris, myocardial infarction (MI), acute and chronic heart failure as well as other conditions such as essential tremor and migraine.[3] Moreover, they have played a primary role in controlling blood pressure (BP) especially in patients with these specific comorbidities and in reducing cardiovascular risk with regard to the composite outcome of death, stroke, and MI among patients younger than 60 years of age.[4,5] In major studies, there was no difference in event rates between those randomly assigned to β-blockers compared with those receiving other antihypertensive agents.[6,7] However, in patients 60 years of age or older, β-blockers were associated with significantly higher rates of stroke, but not MI, heart failure, or death.[8–10] Consequently, the Canadian Hypertension Education Program (CHEP) does not presently recommend the use of β-blockers as first-line

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See page 339 for disclosure information.

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Table 1. Sites of action and physiological effects for the respective β-adrenergic receptors

Receptor	Site of action	Physiological effect
β_1	Heart	↑ Chronotropy, ↑ inotropy, ↑ AV node conduction velocity
	Juxtaglomerular cells	↑ Renin production
β_2	Smooth muscle	↑ Relaxation in vessels, bronchi, gastrointestinal tract, and genitourinary tract
	Skeletal muscle	↑ Glycogenolysis and potassium uptake
	Liver	↑ Glycogenolysis and gluconeogenesis
	Pancreas	↑ Insulin and glucagon secretion
	Thyroid	↑ Conversion of T4 to T3
β_3	Adipose tissue	↑ Lipolysis and thermogenesis

AV, atrioventricular.
Adapted from Mason et al.[3]

therapy in hypertensive patients 60 years of age and older, with the exception of those with coexisting cardiac diseases.[1] Several reports suggest that the lack of consistent outcome data may relate to the use of traditional β-blockers such as atenolol, with their ability only to reduce cardiac output, without beneficial effects on peripheral vascular resistance.[11–13]

Therefore, in order to reassess the place of β-blockers in the armamentarium of hypertension treatment, the present report will present the different pharmacological and clinical properties of β-blockers, as well as their metabolic effects and their usefulness in hypertensive patients. Most of the clinical studies demonstrating the benefits, but also the pitfalls, of β-blockers in hypertension were performed with first- and second-generation β-blocking agents, mainly atenolol. The present report will also discuss the pharmacology of a third generation of β-blocking agents with vasodilating properties such as carvedilol, labetalol, and nebivolol.

Drug Development

During the last 50 years, new techniques involving molecular pharmacology and radioligands have allowed more precise definition of the nature and role of the different subtypes of adrenoreceptors.[14] Using pharmacologic, biochemical, and molecular biological techniques, 3 subtypes of β-adrenergic receptors have now been well characterized.[15] The β_1 receptor is mainly found in the heart, where it represents 75%-80% of the β-adrenoreceptor mass. The β_2 receptor predominates in a number of sites such as lung, uterus, kidney, liver, and peripheral blood vessels. More recently, the β_3 adrenoreceptor has been identified in adipose tissue.[16] The roles and actions of these 3 receptor subtypes have now been well described. Indeed, they promote different actions on different tissues as described in Table 1. Presently, the β_1 and β_2 receptors remain the subtypes of major importance in the clinical setting.

Mechanisms of Action

Pharmacological agents that block β-adrenergic receptors act quite differently depending on the receptor subtypes they target.[15] In general, nonselective agents like propranolol nonselectively block both β_1 and β_2 receptors. By blocking β_1 receptors, they reduce heart rate, nodal conduction velocity, and contractility. On the other hand, by blocking β_2 receptors, they tend to promote vascular smooth muscle contraction and thus to increase peripheral resistance.[17] Second-generation agents such as atenolol, metoprolol, and bisoprolol have relative selectivity for cardiac β_1 receptors.[18] Third-generation agents (which are not pure β-blockers) have added vasodilatory properties, acting chiefly through 2 mechanisms: (1) direct vasodilation, possibly mediated by the release of nitric oxide (NO) as for nebivolol, and (2) added α-adrenergic blockade as in labetalol and carvedilol.[19]

Pharmacological Characteristics

The differences in pharmacological effects introduce the concept that β-blockers represent a very heterogeneous class of antihypertensive agents.[11] Indeed, β-blockers differ with respect to their β_1 receptor selectivity, intrinsic sympathomimetic activity (ISA), membrane-stabilizing activity, lipophilicity, vasodilatory mechanisms and pharmacokinetic characteristics. In clinical practice, β-blockers are selected according to these characteristics. As shown in Table 2, different generations of β-blockers have been developed during the last 60 years. They all possess significant antihypertensive properties. However, differences in mechanism of action will translate into differences in physiologic effects and will modulate not only the way they produce antihypertensive effects but also their tolerability profile. As previously mentioned, the antihypertensive efficacy of conventional nonvasodilating β-blockers resides in their ability to reduce cardiac output.[3,20] A new generation of β-blockers directly reducing peripheral vascular resistance has been developed. These peripheral vasodilatory properties can be obtained by blocking both α- and β-adrenergic receptors (labetalol, carvedilol) or through an increase in NO bioavailability (nebivolol).[19,21] Pharmacodynamic properties will be discussed in the following sections.

Receptor selectivity

Receptor selectivity or cardioselectivity represents an important issue in choosing β-blockers in the clinical setting. It is well known that most of the therapeutic actions are due to β_1-receptor antagonism.[22,23] However, the combined blockade of β_2 adrenoreceptors with β_1 receptors is frequently responsible for many side effects in clinical practice (bronchospasm, etc).[3] Therefore, clinicians will usually select a β-blocker that is highly cardioselective in order to decrease the incidence of untoward effects and maximize the effects on heart rate and accordingly on cardiac output. However, cardioselectivity does not mean "cardiospecificity," Indeed, there is no clinically available agent that specifically blocks the β_1 adrenoreceptor. Cardioselectivity varies among agents but even for the most cardioselective it is greater at lower doses.[11] Indeed, in low doses, agents with β_1 selectivity have less tendency to affect bronchial β_2 receptors. They are also less prone to block the vasodilatory effects mediated by vascular β_2 receptors.[19] With high doses, there is concern that these agents may lose their selectivity for cardiac β_1 receptors. However, a review of the Cochrane collaboration updated in 2011[24] demonstrated that cardioselective agents given at relatively high doses to patients with mild to moderate reversible bronchospastic airway disease or chronic obstructive pulmonary disease produce no reduction in forced expiratory volume in 1 second (FEV1).

Table 2. Pharmacological properties of the different β-blockers

Drug	β_1-Blockade potency ratio	β1/β2 selectivity	ISA	Lipophilicity	MSA	Half-life (h)	Other
Non-selective β-blockers							
Nadolol	1.0	0	0	Low	0	12-24	
Pindolol	6.0	0	++	High	+	3-4	
Propranolol	1.0	0	0	High	++	3-4	
Sotalol	0.3	0	0	Low	0	12	Antiarrythmic effects
Timolol	0.6	0	0	High	0	4-5	
Selective β-blockers							
Acebutolol	0.3	+	+	Moderate	+	3-4	
Atenolol	1.0	+	0	Low	0	6-9	
Bisoprolol	10.0	++	0	Moderate	0	9-12	
Esmolol (IV)	NA	++	0	Low	0	9 min	
Metoprolol	1.0	++	0	High	0	3-4	
α- and β-blockers							
Labetolol	0.3	+	0	Low	0	3-4	α_1-Blocking effect, direct β-vasodilation
Carvedilol	10.0	0	0	Moderate	++	7-10	α_1-Blocking effect
Selective β-blocker with ancillary properties							
Nebivolol	10.0	+++	0	Moderate	0	8-27	Endothelium dependent NO-mediated vasodilation

ISA, intrinsic sympathomimetic activity; IV, intravenous; MSA, membrane-stabilizing activity; NA, not applicable; NO, nitric oxide.
Adapted from Mason et al.,[3] Manrique et al.,[18] and Frishman.[22]

Lipophilicity

Lipophilicity, which relates to the chemically-based lipid solubility of a β-blocker, is an important point to consider because it may influence both efficacy and tolerability. In the context of β-blockers, highly lipophilic agents such as propranolol and metoprolol have been associated with a greater incidence of central nervous system side effects such as nightmares, insomnia, lethargy, confusion, and depression.[18] These untoward effects, which limit the use of those agents, are related to penetration through the blood-brain barrier. More hydrophilic agents such as atenolol are excreted by the kidney and are less prone to produce this kind of untoward effect.[15] On the other hand, choosing a highly lipophilic agent for its significant central nervous system penetration is appropriate when benefit for migraine is desired if associated with hypertension in a specific patient.[18]

Intrinsic sympathetic activity

Another characteristic of the β-blockers that may have a significant clinical effect is ISA. This property also known as partial agonist activity is due to similarity of the agonist and antagonist molecules. Because agonist effect on the β_1 receptor will increase heart rate, agents possessing partial agonist activity may be useful in the context of excessive bradycardia or negative inotropy at rest. Nevertheless, the clinical significance of this characteristic is still a subject of debate.[25,26] Some authors have also suggested neutral effects of this type of β-blocker on plasma lipids.[22]

Membrane stabilizing effect

Some β-blockers have membrane-stabilizing activity at supratherapeutic concentrations.[3] This quinidine-like effect on cardiac action potentials may result in negative inotropy. However, at therapeutic doses, there has been no evidence of this effect, and thus this characteristic is of limited interest in clinical practice.

Ancillary properties of β-blockers

Some new β-blockers share ancillary properties that discriminate them from pure conventional β-blockers and may explain their mechanism of BP reduction as well as their cardioprotective effects.[21,27] These β-blockers demonstrate direct vasodilatory effects. Among them, carvedilol and to a lesser extent, labetalol, have vasodilatory effects mediated by blockade of α-receptors, as well as direct vasodilator activity. Nebivolol promotes vasodilation via the L-arginine-NO-dependent pathway, by increasing NO bioavailability,[3,18,28,29] a mechanism possibly triggered by activation of β_3 receptors.[30] Nebivolol has been demonstrated to both increase NO production via stimulation of endothelial NO-synthase and by reducing oxidative inactivation of NO.[31,32] Several other β-blockers, such as carteolol, have also been shown to increase NO production.[3] This mode of action may be particularly relevant because NO improves endothelial function.[19] Unlike conventional β-blockers, these agents generally display neutral effects on cardiac output while decreasing peripheral vascular resistance and increasing stroke volume.[13,33] A recent study has also shown that these agents may reduce aortic pulse pressure and wave reflection, while their effects on brachial BP and aortic stiffness remain similar to conventional β-blockers.[34] However, the clinical significance of these properties in terms of hard end points has not been studied.

Clinical Efficacy of β-Blockers in Hypertension

Many studies have demonstrated the antihypertensive efficacy of the β-blockers as a class of drugs.[35] In addition, other studies have demonstrated their efficacy in preventing cardiovascular events. In 2006, Khan and McAllister published a meta-analysis based on 21 trials involving more than 145,000 patients[36] in response to the analysis from Lindholm et al.[12] As compared with placebo, β-blockers used as first-line monotherapy reduced major cardiovascular outcomes (composite end point of death, stroke, and MI) in younger patients

(younger than 60 years of age) by 14% (risk ratio [RR], 0.86; 95% confidence interval [CI], 0.74-0.99). In older patients there was a nonsignificant risk reduction of 11% (RR, 0.89; 95% CI, 0.75-1.05). In 1998, a meta-analysis from Messerli et al. reported similar findings in older patients.[17] Antihypertensive treatment using β-blockers was significantly inferior to diuretics on the endpoints of all-cause mortality, coronary heart disease, and cardiovascular mortality. When compared with other active treatments, β-blockers demonstrated similar efficacy vs comparators (RR, 0.97; 95% CI, 0.88-1.07) in younger patients, while they proved to be inferior (RR, 1.06; 95% CI, 1.01-1.10) in older patients. This difference was particularly obvious in the incidence of stroke, which increased with β-blockers in the elderly (RR, 1.18; 95% CI, 1.07-1.30). Since the publication of the Khan et al. meta-analysis, CHEP continues to recommend β-blockers as first-line agents in patients younger than 60 years of age without other compelling indication.[1]

That being said, there is still controversy about β-blockers as first-line treatment agents in hypertension. In 2005, Lindholm et al. published a meta-analysis of 18 randomized studies presenting data on cardiovascular protection associated with β-blockers.[12] This report showed an excess risk of stroke (RR, 1.16; 95% CI, 1.04-1.30) in the β-blocker treated group as compared with other treatments. When these and other major studies results were reanalyzed excluding all β-blockers, except atenolol, the RR increased to 26% (RR, 1.26; 95% CI, 1.15-1.38) approaching the results of Khan and McAllister in elderly patients.[36] However, when excluding atenolol from the model, the RR of stroke was not statistically different (RR, 1.20; 95% CI, 0.30-4.71) between β-blockers and other antihypertensive treatments. Therefore, as opposed to the conclusion of Lindholm et al.,[12] we consider that the paucity of data on β-blockers other than atenolol suggests that it may not be appropriate to extrapolate these findings beyond atenolol. In 2006, the National Institute for Health and Clinical Excellence guidelines concluded that β-blockers, primarily atenolol, were less effective than other classes of antihypertensive agents in reducing events, especially strokes in all age groups.[37]

Therefore, based on these different publications, some authors suggested that some β-blockers (particularly atenolol) might be less protective than others, which may explain their poor performance compared with other classes of agents.[12,17] In this regard, the **C**onduit **A**rtery **F**unction **E**valuation (CAFE),[38] a substudy of the **A**nglo-**S**candinavian **C**ardiac **O**utcomes **T**rial (ASCOT) demonstrated that, for a similar reduction in brachial BP, there was a significantly higher central aortic systolic BP (4.3 mm Hg) with the atenolol-based treatment regimen compared with amlodipine. Because central aortic pressure has been associated with increased vascular events, especially stroke, this could be a partial explanation to explain the excess risk of stroke associated with β-blockers compared with other first-line agents.[39]

Drug Combinations With β-Blockers in Hypertension

As a large proportion of hypertensive patients will frequently require more than 1 medication to obtain BP control,[1,40] physicians should know which antihypertensive agent to combine with β-blockers. In terms of synergistic effects, dihydropyridine calcium channel blockers (DHP-CCB) represent a good selection to combine with β-blockers. On the one hand, the potent vasodilatory effect of DHP-CCB produces reflex tachycardia that can be counteracted by β-blockers. On the other hand, combining β-blockers with non-DHP-CCB should be done with caution because of the increased risk of atrioventricular blockade, especially when combining β-blockers with verapamil. Regarding combinations with angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-receptor blockers (ARBs) and in the absence of compelling indications such as angina or post-MI status, β-blockers may not be an appropriate choice because both classes act on the renin-angiotensin-aldosterone system. In this regard, in the **A**ntihypertensive and **L**ipid-**L**owering Treatment to Prevent **H**eart **A**ttack **T**rial (ALLHAT),[41] atenolol was used as an add-on agent to chlorthalidone, lisinopril, or the DHP-CCB amlodipine. This may explain why systolic BP in the atenolol-lisinopril group was higher by 2 mm Hg compared with the atenolol-chlorthalidone group, and could also account for the higher incidence of complications. Based on the same study, combining β-blockers with thiazide diuretics represents a good treatment strategy.[40,42]

Metabolic Effects of β-Blockers

Since the widespread use of β-blockers in hypertension, the metabolic tolerability profile of these agents has always been of concern. Indeed, abnormalities in glucose and insulin levels as well as in lipid and carbohydrate metabolism have been reported in several publications dealing with the effects of traditional β-blockers in pooled datasets.[19,27] With regard to lipid profile, Kasiske et al. published a meta-analysis of 474 studies regrouping more than 65,000 patients performed between 1966 and 1993,[43] which revealed that β-blockers were associated with a significant decrease in high-density lipoprotein cholesterol.[43] This study also showed a significant increase in triglyceride levels, by a mean of 0.35 mmol/L (95% CI, 0.31-0.39 mmol/L). The effect on triglyceride levels was improved with β-blockers characterized by cardioselectivity and ISA.[26,43] Moreover, agents holding both cardioselectivity and ISA significantly reduced total (−0.14 mmol/L; 95% CI, −0.24 to −0.04 mmol/L) and low-density lipoprotein cholesterol levels (−0.17 mmol/L; 95% CI, −0.28 to −0.07 mmol/L).[43]

The effects of β-blockers on glucose disposal have also been extensively studied. The diabetogenic effect seems to derive from a decrease in pancreatic insulin secretion, increased gluconeogenesis through glycogenolysis secondary to unopposed α_2 activity, and decreased insulin sensitivity secondary to a reduced peripheral blood supply.[44] In a study comparing atenolol and nebivolol, Poirier et al. demonstrated that the conventional cardioselective β-blocker atenolol decreased insulin sensitivity by 20% while nebivolol was neutral as assessed by euglycemic hyperinsulinemic clamp technique.[45] The **C**arvedilol **o**r **M**etoprolol **E**uropean **T**rial (COMET) investigators compared the effects of metoprolol and carvedilol on diabetes in patients with heart failure but no diabetes at baseline.[46] New-onset diabetes was diagnosed significantly less frequently (10.3 vs 12.6%; $P = 0.048$) and diabetic events were significantly less common (10.6 vs 13.0%; $P = 0.039$) in the carvedilol group vs the metoprolol group. These results suggest less detrimental effects of vasodilating β-blockers on glucose

tolerance as compared with cardioselective agents. However, the effect on morbidity/mortality end points is still unknown.

In the ALLHAT trial,[41] the use of thiazide diuretics was associated with an increase in new-onset diabetes. It was also demonstrated that the combination of β-blockers with diuretics increased the frequency of new-onset diabetes.[47] In 2007, Bangalore et al. published a meta-analysis investigating the risk of new-onset diabetes in more than 90,000 patients having been treated with β-blockers but without diuretic treatment.[48] They demonstrated a 22% increased risk (RR, 1.22; 95% CI, 1.12-1.33) of new-onset diabetes compared with other nondiuretic antihypertensive agents. In addition to their negative effect on glucose metabolism, β-blockers have the potential to mask symptoms of hypoglycaemia such as tachycardia and tremor.[19] Finally, because diabetes is an important risk factor for the development of cardiovascular disease, physicians should consider recently published studies demonstrating more beneficial results in favour of other classes of agents. In fact, ACEIs and ARBs in comparison with β-blocker-based treatment regimens[49] and ACEIs combined with DHP-CCB[50] have demonstrated to be superior in decreasing morbidity and mortality. This should guide clinicians through a more cautious use of conventional β-blockers, unless a compelling indication for β-blocker therapy is present.[51]

Side Effect Profile of β-Blockers

Despite compelling evidence for benefits in favour of β-blocker treatment in hypertension and a number of associated conditions, there is an ongoing reluctance for many clinicians to use these agents.[18] This may be due to concerns about tolerability, and mainly to central nervous system side effects like depression, fatigue, nightmares, and sexual dysfunction. One should be cautious when using these agents in patients with asthma or chronic obstructive pulmonary disease because of the risk of bronchospasm, even though the use of β_1-cardioselective agents has been favoured.[24] In addition, cardiac conditions such as sick sinus syndrome, decompensated congestive heart failure with systolic dysfunction, and atrioventricular block greater than first degree are also limitations for the use of these medications.[22]

β-Blockers and Their Role in Heart Disease

MI

Conventional β-blockers have clearly demonstrated their efficacy to reduce mortality after MI. A meta-analysis of 17 studies showed that there is a definite relationship between efficacy to reduce the incidence of MI and the reduction of heart rate at rest.[28] This may explain why β-blockers with ISA have not shown efficacy in preventing new events.[26]

Angina pectoris

CHEP recommends conventional β-blockers as the treatment of choice in hypertension associated with angina pectoris.[1] In fact, the reduction of heart rate induced by β_1-receptor blockade permits a reduction in myocardial oxygen demand resulting in cardiac protection.[22]

Congestive heart failure

β-blockers are 1 of the mainstay therapies in heart failure because they antagonize the deleterious effects of chronic activation of the sympathetic nervous system. They also exert an antiarrythmic effect coupled with decreased BP and heart rate.[52] A number of studies have demonstrated the beneficial effects of β-blockers in reducing mortality in patients with congestive heart failure. Three β-blockers, bisoprolol,[53] metoprolol,[54] and carvedilol[55] have shown a relatively constant risk reduction of 30% in terms of the composite end point of all-cause mortality and cardiovascular hospital admissions. More recently, the **S**tudy of the **E**ffects of **N**ebivolol **I**ntervention on **O**utcomes and **R**ehospitalization in **S**eniors With Heart Failure (SENIORS) showed a less pronounced (14%) decrease in this composite endpoint, with a nonsignificant decrease of 12% in all-cause mortality.[52] Therefore, conventional β-blockers should be the treatment of choice in hypertension associated with heart failure.[1] Of note, the recommendation states to use them in combination with ACEIs or ARBs.

Are All β-Blockers Equally Effective in Hypertension?

Most authors consider the antihypertensive effect of the different β-blocking agents to be equal when administered at equipotent doses.[56] Characteristics of cardioselectivity, duration of action, lipophilicity, and ISA may affect efficacy and tolerability. In the clinical setting, clinicians should choose a specific agent to optimize the tolerability profile (cardioselective agent vs asthma or Raynaud's phenomenon; less lipophilic agent vs central effects such as fatigue, insomnia; agent with ISA vs excessive bradycardia at rest, etc). However, no published studies demonstrate that specific β-blockers are superior in terms of outcome data. Nevertheless, as discussed previously in the present report, some data seem to discourage the use of atenolol. There is still an open debate on the use of β-blockers as first-line agents in the treatment of hypertension. CHEP reviews its clinical recommendations annually and is critical about the use of β-blockers as first-line treatment agents in patients older than 60 years of age.[1]

Conclusion

For many years, β-blockers have been used for the treatment of hypertension, for which they are clearly effective. Meta-analyses have also shown that they are effective in reducing cardiovascular events, especially in patients younger than 60 years of age. However, the mechanism of action of conventional β-blockers depends largely on reducing heart rate and cardiac output, which may not be optimal because there is little effect on peripheral vascular resistance, the primary abnormality in essential hypertension. Consequently, a number of studies and consensus guidelines question the place of conventional nonvasodilating β-blockers as first-line treatment agents in hypertension. Recently, the availability of β-blockers possessing vasodilating properties has generated interest because they preserve cardiac output and target peripheral vascular resistance. However, lack of outcome data limits the use of these new agents in clinical practice. Finally, as recommended by CHEP, β-blockers are still considered first-line treatment agents in hypertension for younger patients (younger than 60 years of age) and for those with an MI or heart failure.

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