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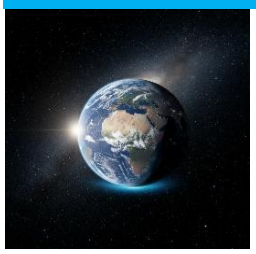

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Beta-Adrenoceptor Antagonists and the Physiological Response to Exercise: Clinical Implications for Training and Rehabilitation

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Abstract

Aim: This narrative review aimed to analyze the impact of beta-adrenoceptor antagonists on the physiological response to exercise and to identify clinical implications for exercise training prescription and exercise-based rehabilitation in patients receiving long-term pharmacotherapy.

Material and Methods: A structured literature search was conducted in PubMed, Embase, and the Cochrane Library for studies published between January 2018 and February 2026. Randomized controlled trials, crossover studies, observational research, and relevant systematic reviews evaluating the effects of cardioselective and non-selective beta-adrenoceptor antagonists on peak oxygen uptake (VO_2peak), heart rate response, and ventilatory thresholds in healthy and clinical populations were included. Due to heterogeneity in study design, populations, and pharmacological regimens, findings were synthesized narratively without quantitative meta-analysis.

Results: Beta-adrenoceptor antagonists consistently attenuate the chronotropic response to exercise, typically reducing maximal heart rate by approximately 18–19%. Despite this effect, VO_2peak and maximal power output are often preserved through compensatory mechanisms such as increased stroke volume and enhanced arteriovenous oxygen extraction. Under beta-blockade, the relationship between heart rate and external workload becomes blunted, limiting the reliability of heart rate–based methods (e.g., %HRmax, HRR) for exercise intensity prescription.

Conclusions: Exercise-based rehabilitation in patients treated with beta-adrenoceptor antagonists requires an individualized, physiology-guided approach. Cardiopulmonary exercise testing with determination of ventilatory

thresholds (VT1 and VT2) should be preferred for exercise prescription. In settings without access to CPET, subjective measures such as the Borg Rating of Perceived Exertion scale and the talk test should be incorporated to ensure safety and training effectiveness.

Keywords: beta-blockers; beta-adrenoceptor antagonists; exercise capacity; VO_2peak; cardiopulmonary exercise testing; ventilatory threshold

1. Introduction

Physical activity and appropriately prescribed training tailored to an individual patient's needs constitute key components of health prevention and rehabilitation. Contemporary physiotherapy and sports medicine increasingly provide care for physically active individuals who are simultaneously receiving long-term pharmacotherapy. Beta-adrenoceptor antagonists (beta-blockers) are medications widely used in clinical practice to treat conditions such as heart failure, arterial hypertension, and atrial fibrillation [1,13,15,19,20,31]. Beta-adrenoceptor antagonists act by inhibiting beta-adrenergic receptors, thereby affecting cardiovascular function [6]. This results, inter alia, in a reduction in heart rate, decreased myocardial contractility, and attenuation of sympathetic nervous system responses to exercise stress. Although these mechanisms are beneficial for treating cardiac disease, they may also concurrently affect exercise tolerance, exercise capacity, and the subjective perception of fatigue. In clinical and physiotherapeutic practice, the use of beta-adrenoceptor antagonists poses important challenges for exercise training prescription and exercise-based rehabilitation. Standard methods of exercise intensity control based on heart rate may not reflect the actual physiological load in patients receiving beta-adrenoceptor antagonists. Consequently, alternative strategies for monitoring exertion are required, including ratings of perceived exertion, analysis of ventilatory parameters, and individualization based on exercise thresholds. This paper aims to analyze the impact of beta-adrenoceptor antagonists on the exercise response and to discuss clinical implications for exercise training and rehabilitation planning.

2. Methodology

This work was conducted as a narrative review of literature. The aim of the review was to evaluate the effects of beta-adrenoceptor antagonists on the physiological exercise response and to identify clinical implications for exercise training prescription and exercise-based rehabilitation planning. The literature search was performed in PubMed, Embase, and the Cochrane Library, using combinations of the following terms: beta-blockers, exercise capacity, CPET, heart rate response, exercise training, and ventilatory threshold. The search covered publications from January 2018 to February 2026. In addition, reference lists of key articles were hand-searched. Publications in English and Polish were included. Owing to heterogeneity across studies (different populations, drugs, doses, and exercise protocols), findings were synthesized narratively without quantitative meta-analysis.

3. Mechanisms of Action of Beta-Adrenoceptor Antagonists

Adrenergic receptors constitute a heterogeneous group of membrane receptors that are classified into two principal types: alpha-adrenergic receptors (α1 and α2) and beta-adrenergic receptors (β1, β2, and β3) [2,3,20, 27-30]. Activation of most of these receptors occurs under the influence of noradrenaline, the key neurotransmitter of the sympathetic nervous system.

Noradrenaline is synthesized and released primarily from sympathetic nerve terminals, whereas the adrenal medulla secretes predominantly adrenaline and, to a lesser extent, noradrenaline [3]. Beta-adrenoceptor antagonists interact with beta-adrenergic receptors as competitive antagonists of endogenous catecholamines such as noradrenaline and adrenaline. Depending on receptor subtype selectivity, cardioselective and non-selective agents are distinguished. β1 receptors, of greatest clinical relevance to the cardiovascular system, are located mainly in cardiomyocyte membranes. Pharmacological β1 blockade induces functional cardiac changes that are exploited in cardiovascular therapy, as summarized in Table 1. Physiological stimulation of β1 receptors—mainly by noradrenaline released from sympathetic endings or circulating adrenaline—activates adenylate cyclase, leading to increased intracellular cyclic adenosine monophosphate (cAMP) concentration in cardiomyocytes [7]. Elevated cAMP enhances calcium influx into cardiac muscle cells, increasing contractile force (positive inotropic effect) and myocardial oxygen demand. Concurrently, heart rate accelerates through increased sinoatrial node automaticity and improved atrioventricular nodal conduction, resulting in positive chronotropic and dromotropic effects [19]. The literature also distinguishes beta-adrenoceptor antagonists with additional vasodilatory properties (often referred to as 'third-generation' agents), which—beyond classical β-receptor blockade—exert vasodilatory effects. This feature is used, among others, in the treatment of arterial hypertension. Examples include carvedilol, whose vasodilatory effect results from concomitant α1-receptor blockade, and nebivolol, which promotes vasodilation by increasing nitric oxide bioavailability in the vascular endothelium.

Table 1. Hemodynamic effects of beta-adrenoceptor antagonists and exercise-related implications

Effect	**Direct cardiac effect**	**Clinical and exercise-related implications**
Negative chronotropic effect	Reduction in heart rate through inhibition of sinoatrial node activity	– Lower resting and exercise heart rate; [27,28] – Blunted HR increase during exercise; – Reduced utility of HR as an indicator of training intensity [10]
Negative inotropic effect	Reduction in myocardial contractile force and cardiomyocyte contractility	– Potential reduction in stroke volume and cardiac output; – Potential reduction in exercise tolerance; – Beneficial effects on myocardial oxygen balance [10]
Negative dromotropic effect	Slowing of impulse conduction through the atrioventricular node	– Possible limitation of rapid cardiac adaptation to abrupt changes in workload
Negative bathmotropic effect	Reduced myocardial excitability via an increased depolarization threshold	– Electrical stabilization of the heart; – Reduced risk of exercise-induced arrhythmias
Effect on cardiac output	Limitation of the rise in cardiac output during physical exertion	– Earlier onset of fatigue at higher intensities in some individuals; – Need for individualized training loads
Effect on the exercise response	Flattening of the physiological cardiovascular response to exercise	– Need for alternative methods of intensity monitoring (Borg scale, talk test, CPET) [18]

4. Changes in Physical Fitness in Individuals Receiving Beta-Adrenoceptor Antagonists

Studies (Priel et al., 2021 [4]) indicate that the use of beta-adrenoceptor antagonists, despite a pronounced attenuation of the chronotropic response during exercise, does not necessarily lead to a clinically meaningful deterioration in exercise performance assessed by maximal power output. The observed reduction in heart rate by approximately 18–19% is a direct consequence of the pharmacodynamic mechanism of this drug class, yet it can be effectively compensated by other components of the cardiorespiratory response. An important adaptive mechanism appears to be an increase in stroke volume and an increase in the arteriovenous oxygen extraction difference, reflected by an increase in oxygen pulse (VO_2/HR). Through these mechanisms, it may be possible to maintain comparable oxygen uptake at a given workload up to maximal exercise. This suggests that limiting maximal heart rate is not the sole determinant of exercise tolerance, and that the organism retains substantial compensatory capacity under beta-blockade. The absence of clinically significant disturbances in muscle strength, ventilatory parameters, and gas exchange further supports that, in the studied population, beta-adrenoceptor antagonists did not adversely affect peripheral determinants of exercise capacity. These findings challenge the widespread assumption of a uniformly detrimental effect of beta-blockers on exercise tolerance, indicating that the magnitude of this effect depends on the studied population, the specific agent, and the severity of the underlying disease.
From a clinical perspective, these observations are relevant because they suggest that in some patients—particularly those without marked chronotropic incompetence—therapy with beta-adrenoceptor antagonists may be continued without major concern about a substantial reduction in the ability to engage in physical activity. At the same time, they highlight the need for individualized assessment of exercise tolerance, especially in individuals whose cardiovascular adaptive reserve may be limited. In a systematic review and meta-analysis (Montero et al., 2018 [5]) including 14 randomized controlled trials with 616 patients with heart failure, long-term therapy with beta-adrenoceptor antagonists (3–24 months) did not significantly affect peak oxygen uptake ($\dot{V}O_2$peak), regardless of intervention characteristics. Maximal exercise capacity also remained unchanged despite an improvement in New York Heart Association (NYHA) functional class. Despite a significant reduction in maximal heart rate, $\dot{V}O_2$peak was preserved, indicating effective hemodynamic compensation during chronic beta-blockade.

In a randomized experimental study, the effects of a single dose of 5 mg bisoprolol and 40 mg propranolol, compared with placebo, on physiological parameters and sports performance in archers were assessed. The experiment demonstrated a statistically significant reduction in heart rate in athletes receiving beta-adrenoceptor antagonists, with a more pronounced effect after bisoprolol. Despite the observed reduction in heart rate, no significant improvement in sports performance (shot accuracy) was found. An initial analysis suggested lower scores in the propranolol group; however, after statistical correction, these differences were no longer significant. This indicates that pharmacologically induced heart-rate reduction did not translate into improved precision in the sports task. Furthermore, no significant differences in stabilometric parameters, including centre of pressure (CoP) sway, were identified between trials with beta-adrenoceptor antagonists and placebo. These findings suggest that reduced sympathetic activity and heart rate did not meaningfully affect postural control or stability during the task. Nevertheless, it should be emphasized that the study involved a small sample size, limiting statistical power and generalizability. Therefore, further studies with larger samples and more diverse athlete populations are warranted to clarify the potential influence of beta-adrenoceptor antagonists on performance in precision sports.

5. Comparison of Cardioselective and Non-Selective Beta-Adrenoceptor Antagonists

Beta-adrenoceptor antagonists currently used in clinical practice constitute a heterogeneous pharmacological group. Individual agents differ, inter alia, in the degree of β_1 selectivity, lipophilicity, and the presence of intrinsic sympathomimetic activity (ISA). These differences may be clinically important for individualized drug selection, especially in patients with comorbidities. Beta-adrenoceptor antagonists are classified as cardioselective or non-selective (Table 2) according to their selectivity for beta receptors. Some agents also exhibit partial intrinsic sympathomimetic activity (ISA). Cardioselective beta-adrenoceptor antagonists preferentially block β1 receptors, whereas non-selective agents block both β1 and β2 receptors [8–11]. Cardioselective agents typically exert less direct influence on β2 receptors in the bronchi and vasculature, which may be relevant in patients with obstructive airway disease. At the same time, it should be emphasized that effects on peripheral hemodynamics may also occur indirectly (e.g., through neurohormonal mechanisms), and therefore statements suggesting no influence on vascular resistance should be formulated cautiously [7].

Table 2. Examples of beta-adrenoceptor antagonists by pharmacodynamic profile (illustrative classification)

First generation – non-selective	**Second generation – cardioselective**	**Third generation – with additional vasodilatory effects**
propranolol	metoprolol	carvedilol
sotalol	esmolol	celiprolol
timolol	bisoprolol	nebivolol
pindolol	betaxolol	labetalol
carteolol	atenolol	
nadolol	acebutolol	

6. Clinical Implications of Selecting Beta-Adrenoceptor Antagonists in the Context of Training and Rehabilitation

6.1. The Role of CPET in Exercise Assessment under Beta-Blockade

Cardiopulmonary exercise testing (CPET) is increasingly used in chronic cardiac disease and in apparently healthy individuals with unexplained dyspnea. It was applied in the study by Forton et al. (2022). That trial was a randomized, crossover, double-blind, placebo-controlled experiment conducted in active, healthy young adults. Participants performed three CPETs under placebo and two doses of the cardioselective beta-adrenoceptor antagonist bisoprolol (2.5 mg and 5 mg), allowing assessment of the effects of acute β_1 blockade on exercise and hemodynamic parameters. A significant dose-dependent reduction in heart rate and arterial blood pressure was demonstrated both at rest and during maximal exercise. At the same time, no significant changes in VO_2max or maximal power output were observed compared with placebo. These results indicate that selective β_1 receptor blockade substantially modifies the chronotropic and hemodynamic response to exercise without necessarily reducing aerobic capacity. From a clinical perspective, this implies that cardioselective beta-adrenoceptor antagonists may affect the interpretation of cardiovascular parameters during exercise testing and training prescription while relatively preserving VO_2max.

6.2. Determining Training Intensity in Individuals Receiving Beta-Adrenoceptor Antagonists

A key element of any training plan is the appropriate determination of exercise intensity [18]. The percentage of maximal heart rate (%HRmax) and heart rate reserve (%HRR) are commonly

used indices for prescribing intensity. In the study by Birnbaumer et al. (2021) [6], the authors indicated that heart rate–based methods are prone to error and have limited accuracy in patients receiving beta-adrenoceptor antagonists.
Hansen et al. (2022) suggested that, to avoid limitations related to peak-intensity indices in training prescription, recommendations should be based on the first (VT1) and second (VT2) ventilatory thresholds. VT1 corresponds to the intensity at which blood lactate begins to rise while metabolic balance is relatively preserved, whereas VT2 denotes the point of rapid metabolite accumulation and a disproportionate rise in ventilation relative to CO_2 production. These thresholds can be determined from ventilatory and gas-exchange relationships during CPET and then used to define training zones.
Unlike maximal parameters, VT1 and VT2 are attainable for most patients with cardiovascular disease and may provide a more functional basis for individualized training prescription. However, methodological limitations must be considered, including inter-observer variability and difficulties in clearly identifying thresholds in some patients. An additional challenge is translating incremental-test results into constant-load training, which may require practical adjustment of workload prescriptions. Evidence indicates that threshold-based exercise prescription may yield superior improvements in VO_2peak compared with strategies relying exclusively on peak-derived intensity markers. Practical limitations include the availability of ergospirometry; therefore, in resource-limited settings the minimal standard remains an exercise ergometry test, whereas the optimal approach is CPET with VT determination. When determination of exercise intensity based on conventional exercise testing or CPET is not feasible, training planning may rely on subjective methods of exertion assessment such as the Borg scale and practical tools such as the talk test [18].

7. Limitations

This narrative review has several limitations that should be considered when interpreting the findings. First, the included studies exhibited substantial heterogeneity of populations (healthy individuals, athletes, patients with heart failure, and patients with coronary artery disease), which limits direct extrapolation of conclusions to a single homogeneous clinical group. Additional variability resulted from differences in the type of beta-adrenoceptor antagonists used, dosing regimens, and treatment duration (acute administration vs. chronic therapy), making it difficult to define class effects unequivocally.

Another important limitation is the diversity of exercise protocols and methods used to assess exercise capacity parameters, including VO_2peak and ventilatory thresholds, which reduces comparability across studies. Some analyses involved small sample sizes, limiting statistical power and generalizability. Moreover, due to methodological heterogeneity, no quantitative meta-analysis was performed, which increases the risk of interpretive bias characteristic of narrative syntheses. Consequently, the presented conclusions should be interpreted cautiously, and further well-designed randomized studies are needed to clarify the effects of different classes of beta-adrenoceptor antagonists on exercise adaptations and rehabilitation strategies.

8. Discussion and Summary

The aim of this review was to analyze the impact of beta-adrenoceptor antagonists on the physiological exercise response and to identify clinical implications for exercise training and rehabilitation planning. The available evidence indicates that, although beta-adrenoceptor antagonists substantially modify the chronotropic and hemodynamic response to exercise, their

effect on global aerobic capacity, expressed as VO_2peak, is not uniformly negative. The most consistent pharmacological effect of beta-adrenoceptor antagonists is a reduction in heart rate both at rest and during maximal exercise. This phenomenon limits the applicability of standard training-intensity methods based on %HRmax or heart rate reserve (HRR). In beta-blocked populations, the relationship between heart rate and external workload becomes flattened, which can lead to underestimation of actual exercise intensity when traditional training formulas are applied. At the same time, several studies have shown that despite a significant reduction in maximal heart rate, peak oxygen uptake (VO_2peak) may be preserved. This is explained by compensatory increases in stroke volume and the arteriovenous oxygen extraction difference. Thus, blunting of the chronotropic response does not necessarily translate into a clinically meaningful deterioration in exercise tolerance, particularly in patients without advanced heart failure. In patients with chronic heart failure, findings are more variable and may depend on the degree of circulatory dysfunction and the specific agent used. An important issue remains the differentiation of effects between cardioselective and non-selective beta-adrenoceptor antagonists. Available data suggest that β_2 receptor blockade may additionally affect vascular responses and exercise metabolism, potentially amplifying limitations in exercise tolerance. However, current evidence does not allow a definitive conclusion regarding the clinical superiority of one class over the other in terms of training adaptations, highlighting the need for further high-quality studies. In clinical practice, the method used to determine training intensity is of particular importance. Evidence confirms the limited utility of maximal parameters (HRpeak, %VO_2peak) in individuals receiving beta-adrenoceptor antagonists. An alternative with higher clinical potential appears to be the use of ventilatory thresholds (VT1 and VT2), which are less dependent on chronotropic response and may serve as a more stable reference for individualized training prescription. Nevertheless, ventilatory-threshold identification is subject to inter-observer variability and requires CPET, limiting widespread implementation. In settings with limited access to ergospirometry, subjective methods such as the Borg scale and the talk test may be applied, particularly when combined with monitoring of clinical symptoms. A multimodal approach combining objective and subjective indicators appears to be the most rational strategy for exercise-based rehabilitation planning in patients receiving beta-adrenoceptor antagonists.

In summary, beta-adrenoceptor antagonists significantly alter the cardiovascular response to exercise; however, their impact on aerobic capacity is complex and dependent on multiple clinical factors. Exercise training and rehabilitation planning in individuals treated with beta-adrenoceptor antagonists should recognize the limitations of methods based solely on heart rate and should prefer individualized strategies based on ventilatory thresholds or combined approaches.

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AI-assisted tools were used exclusively for linguistic refinement and structural editing of the manuscript. The authors take full responsibility for the scientific content, interpretation of the data, and final version of the manuscript.

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