

Pharmacology of Propranolol as an Antihypertensive Drug

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ABSTRACT

Propranolol, a non-selective beta-adrenergic receptor antagonist, has long been used in the treatment of hypertension. It lowers blood pressure through several mechanisms, including reducing heart rate, myocardial contractility, and inhibiting renin release. Despite newer antihypertensive agents, propranolol continues to play a role, particularly in patients with concomitant cardiovascular conditions. This review examines its pharmacological mechanisms, clinical effectiveness, side effects, and its ongoing relevance in hypertension management.

Keywords- Propranolol, Beta-blockers, Hypertension, Pharmacology, Renin-angiotensin system.

I. INTRODUCTION

The force that the body's circulating blood applies to its arterial walls is known as blood pressure. The drugs which lower the blood pressure is commonly known as antihypertensive drugs. That is the most frequent persistent medicative disorders, Bp, is characterized by a continual increase in pressure of artery. (1) It is well known that people with high blood pressure are increasing prone to emerge CVD than people with low blood pressure. The term "silent killer" is frequently used to describe hypertension as the symptoms of bp are absent. High blood pressure harms many organs over time and can lead to various cardiovascular diseases such as angina and stroke. It is a common cause of premature death and causes chronic renal damage, and stroke (2).

Two measurements are used to determine bp

- **Systolic blood pressure, or SBP:** - The force that blood applies to artery walls during heartbeat.
- **Diastolic blood pressure, or DBP:** - Diastolic bp is a typical way to express pressure when the heart relaxes.

Hypertension is a prevalent global health issue, contributing to a range of cardiovascular complications. While beta-blockers like propranolol were once the first-line treatment, their role has evolved with the advent of newer medications. Propranolol, a non-selective beta-blocker, still holds value in the management of hypertension, particularly in specific cases where it offers additional benefits, such as in patients with cardiovascular comorbidities. This paper explores the pharmacology of propranolol, its clinical use, limitations, and its place in modern antihypertensive therapy.(3,4).

II. TYPES OF HYPERTENSIONS

Hypertension is characterized by two types.

- A Primary hypertension
 - B Secondary hypertension
- A. Primary hypertension:-** Primary hypertension, sometimes referred to as essential hypertension or idiopathic hypertension, affects 90% to 95% of the population (5). Essential hypertension is the main cause

of cardiovascular disease for a massive population around the world, and the incidence rate is increasing everyday (WHO, 2008). Some of the important features of primary or essential hypertension are.

1. There is a 40–60% increase in mean arterial pressure (MAP).
2. The renal blood flow is approximately 50% less than normal in the later stages.
3. There is 2-4 times increase in the resistance to blood flow through the kidney.
4. Insufficient arterial pressure will prevent the kidneys from excreting adequate salt and water.

(B) Secondary hypertension: - An etiology-specific kind of hypertension is referred to as secondary hypertension. Here, the disease's underlying cause can be found and treated significantly to lower blood pressure. Additionally, it is classified as-

- **Renal parenchymal hypertension:-** Renal parenchymal hypertension is a well-known secondary hypertension caused by issues with renal parenchyma (6). estimated that it affects 2-5% of people with hypertension. It largely results due to increased Sodium – Na^+ retention (increased salt sensitivity), excessive RAS activation, and sympathetic-excitation.
- **Renovascular hypertension:-** Renal vascular hypertension is due to renal artery stenosis. Renovascular hypertension is primarily caused by RAS overactivation in the kidney (7). The occurrence of renal artery stenosis is anticipated to be about 2% (8) and the renal artery stenosis is mostly caused by atherosclerosis (7).
- **Endocrine hypertension:-** A few of the conditions that result in excessive hormone secretion and Primary aldosteronism- results Na^+ retention, Cushing's disease, and pheochromocytoma are all causes of endocrine hypertension (9). The occurrence of primary aldosteronism in hypertensive patients is reported to be 5% and in patients with other complications is 20% (8).
- **Drug induced hypertension:-** When taken together, drugs like cyclosporine, erythropoietin, glucocorticoids, glycyrrhizin preparations, NSAIDs, oral contraceptives, and sympathomimetic drugs have been shown to increase blood pressure and stop antihypertensive drugs from producing their desired effects in the body.

III. PHARMACOLOGICAL MECHANISMS OF PROPRANOLOL

3.1 Beta-Adrenergic Blockade:-

Propranolol is a nonselective beta-adrenoreceptor antagonist, also classified as a class II antiarrhythmic. It exerts its response by competitively blocking beta-1 and beta-2 adrenergic stimulation in the

heart, which is typically induced by epinephrine and norepinephrine. (9).

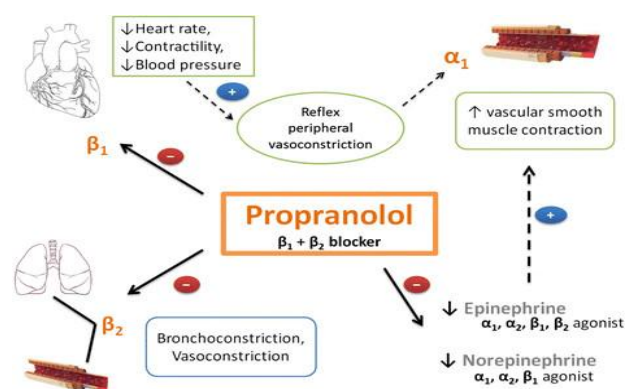
Propranolol primarily exerts its effects through beta-adrenergic blockade.

β_1 Receptor Blockade (Heart): By blocking β_1 receptors in the heart, propranolol decreases heart rate (negative chronotropy) and myocardial contractility (negative inotropy), which leads to a reduction in cardiac output and, ultimately, blood pressure (10).

β_2 Receptor Blockade (Vascular Smooth Muscle): Although the blockade of β_2 receptors can lead to vasoconstriction in certain vascular beds, this effect is generally overshadowed by other mechanisms, making propranolol effective in managing hypertension (11).

Beta-1 receptors are present on cardiac myocytes, including the sinoatrial and atrioventricular nodes. When there is an activation of these receptors, there is an increase in cyclic AMP, which leads to increased intracellular calcium. This process leads to increased contractility of muscle fibers. When there is a blockage of beta-adrenergic receptors, this results in an overall decreased workload of the heart, which leads to subsequent reduced oxygen demand and myocardial remodeling.(12)

Beta-2 receptor activation, on the other hand, leads to increased cyclic AMP that activates protein kinase A, leading to the relaxation of smooth muscle cells in a variety of organs and vessels. Therefore, when beta-2 receptors are blocked, this leads to a small amount of vasoconstriction. This effect can make the use of emergency epinephrine in asthmatics quite problematic, as it blocks the receptors that epinephrine would potentially bind to in the lungs(13). Beta-blockers are highly protein-bound and are well distributed throughout the body with a (volume of distribution) V_D of about 4 to 6L/kg.(13).



3.2 System of Renin-Angiotensin:-

The system of renin angiotensin is majority of blood pressure is significantly influenced by the endocrine system. When a person consumes less salt or when their glomeruli are under perfusion, their kidney's juxtaglomerular apparatus secretes renin. Additionally, it is released in reaction to the sympathetic nervous system being activated. (14).

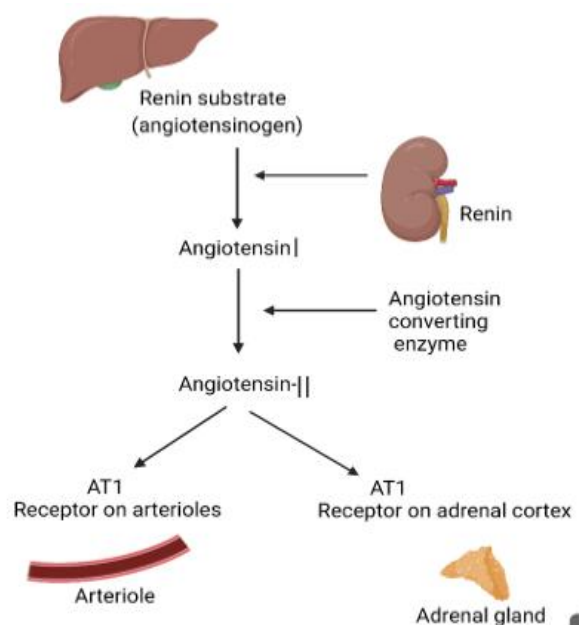


Fig:- Effects of the RAS on hypertension and aldosterone production.

3.3 Reduction of Renin Secretion

Another critical mechanism by which propranolol lowers blood pressure is by inhibiting renin secretion.

Propranolol reduces renin release from the juxtaglomerular apparatus in the kidneys, leading to decreased levels of angiotensin II and aldosterone, both of which contribute to elevated blood pressure via vasoconstriction and sodium retention (15).

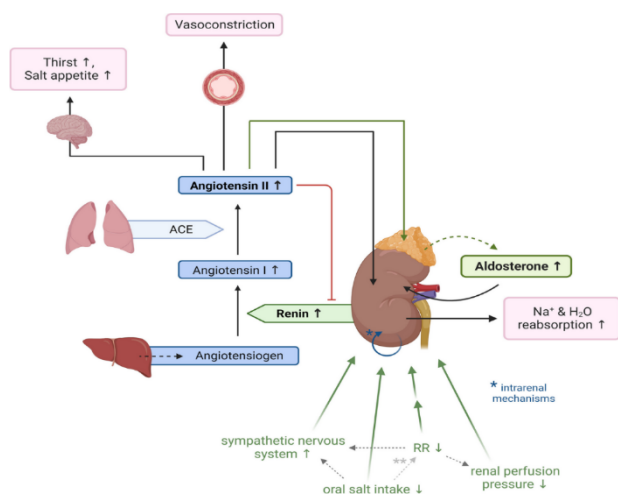


Fig:- vasoconstriction and sodium retention

Central Nervous System Effects

Propranolol is also known to cross the blood-brain barrier, which allows it to reduce central sympathetic outflow. This contributes further to its blood pressure-lowering effects, especially in conditions like anxiety, where its central action helps manage both physical and emotional stress responses (16).

1. Clinical Efficacy in Hypertension

Propranolol is not as widely used as a first-line anti-hypertensive today, given the availability of more selective agents, but it remains invaluable in specific clinical scenarios. It is particularly useful in patients with co-existing coronary artery disease, migraine prophylaxis, hyperthyroidism, and pheochromocytoma.

- **Hypertension and Coronary Artery Disease:** Propranolol reduces myocardial oxygen demand and protects against ischemia in patients with both hypertension and coronary artery disease (17)
- **Migraine Prophylaxis:** Propranolol has shown efficacy in preventing migraine attacks, a benefit that extends beyond its use in hypertension (17).
- **Hyperthyroidism:** In hyperthyroid patients, propranolol controls adrenergic symptoms like tachycardia, palpitations, and tremors, offering symptomatic relief (18).

IV. COMMON SIDE EFFECTS

Common side effects of using propranolol include bradycardia, gastrointestinal issues, abdominal pain, nausea, erectile dysfunction, and wheezing/bronchospasms. (19) Propranolol use can also cause drowsiness, fatigue, and cold extremities. Some extreme side effects to be aware of include allergic reactions, insulin resistance, and hallucinations. Prescribers need to explain and discuss all of the side effects before giving patients a prescription for propranolol (20).

V. ADVERSE EFFECTS AND LIMITATIONS

While propranolol is an effective anti-hypertensive, its use is not without risks. Common adverse effects include:

5.1 Cardiovascular Side Effects: Bradycardia and Hypotension – Excessive beta-blockade can result in dangerously low heart rate and blood pressure (21). This is particularly concerning in patients with pre-existing heart conditions.

5.2 Respiratory Effects: Bronchoconstriction – Due to its non-selective nature, propranolol can induce bronchoconstriction, making it unsuitable for patients with asthma or chronic obstructive pulmonary disease (COPD) (18).

5.3 Metabolic Effects: Hypoglycemia Risk – In diabetic patients, propranolol may mask the symptoms of hypoglycemia, potentially leading to delayed recognition and treatment of low blood sugar (19).

VI. TOXICITY

Ingestion of greater than 1 g of propranolol in 24 hours can potentially be lethal and lead to profound

bradycardia, bradyarrhythmia, hypotension, bronchospasm.

When suspecting a beta-blocker overdose, a patient should always receive glucagon immediately. Glucagon has shown to be very effective in reversing beta-blocker overdose, increasing heart rate, and myocardial contractility. (22).

VII. ENHANCING HEALTHCARE TEAM OUTCOMES

The interprofessional healthcare team includes the patient, the physician, the nurse, certified nurse's aid, and the pharmacist, all working in concert to optimize the patient's health. Therefore, all team members must remain up to date with literature on medication and potential side effects. Furthermore, they must utilize excellent communication skills between the different disciplines to ensure the desired outcome for their patient. A proper history and continuous physical assessments will need to be performed by the health care team to ensure that propranolol is used correctly, with appropriate precautions maintained in at-risk populations to minimize adverse outcomes. Nurses can offer counsel to the patients on their dosing regimen. The pharmacist can check for potential interactions, reinforce the nurse's counsel, answer patient questions, and report any concerns to the prescriber. This interprofessional approach will yield better therapeutic outcomes when using propranolol (23).

VIII. FUTURE PERSPECTIVES

Although propranolol is not a first-line drug for hypertension anymore, it continues to be useful in selected populations. Future research may explore:

Selective β_1 -blockers (e.g., metoprolol) that might reduce the risk of adverse effects like bronchoconstriction, making them more suitable for a broader patient population (24).

New formulations, such as modified-release versions of propranolol, could potentially reduce side effects while maintaining its efficacy in blood pressure management (25).

IX. CONCLUSION

Propranolol remains a valuable antihypertensive agent, especially in patients with comorbid conditions like coronary artery disease and hyperthyroidism. While it has been largely superseded by more modern therapies, its unique pharmacological properties and broad therapeutic applications ensure its continued role in clinical practice. As research continues, propranolol's use may expand, with a focus on optimizing its profile for better safety and efficacy in managing hypertension.

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