Propranolol

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Continuing Education Activity

Propranolol can be used to ameliorate the sympathetic response in angina, tachyarrhythmias, prevention of acute ischemic attacks, migraine prophylaxis, and restless leg syndrome. Propranolol can be used in almost all cases if the desired result is to slow contractility and decrease a patient's heart rate. Propranolol is also used off-label in a variety of other cases, for instance, in performance anxiety, which is a subset of social phobia, a psychiatric condition whose symptoms also include tachycardia, sweating, and flushing secondary to the activation of the sympathetic nervous system. This activity examines the indications, dosing, contraindications, mechanism, and management of propranolol therapy by the interprofessional healthcare team.

Objectives:

- Identify the mechanism of action of propranolol.
- Describe the possible adverse effects of propranolol.
- Review the appropriate monitoring for patients taking propranolol.
- Summarize interprofessional team strategies for improving care coordination and communication to advance Propranolol and improve outcomes.

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Indications

Propranolol is a competitive beta-adrenergic receptor antagonist devoid of agonist activity, making it the prototype for comparison to other beta-antagonists. A British scientist, Sir James Black, first developed propranolol for the treatment of angina pectoris. Over the following years, propranolol started to gain recognition in the treatment of a variety of cardiovascular and noncardiovascular disease processes, making it a widely used pharmaceutical drug.

B-adrenoreceptor antagonists, including propranolol, have been advised to be used for the treatment of heart failure, atrial fibrillation, and coronary artery disease. Furthermore, they have been demonstrated to improve mortality and morbidity in those with hypertension complicated with heart failure, angina, or any history of previous myocardial infarctions. Propranolol can also enhance the sympathetic response in angina and tachyarrhythmias while also preventing acute ischemic attacks. It is also a critical drug used in the treatment of hyperthyroid-induced thyrotoxicosis.

Propranolol not only has extensive use in cardiovascular disease, but it also has several implications in the treatment of noncardiovascular disease processes. It is used as a means of migraine prophylaxis, treatment of restless leg syndrome, essential tremors, and has even been of great success in treating infantile hemangioma.

Off-label use of propranolol includes performance anxiety, which is a subset of a social phobia presenting with tachycardia, sweating, and flushing that occurs secondary to increased activation of the sympathetic nervous system.

The extensive use of propranolol in the medical field highlights the vast importance of the discovery of the drug to society.

Mechanism of Action

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.

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.

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. Beta-blockers are highly protein-bound and are well distributed throughout the body with a Vd of about 4 to 6L/kg.

Administration

Like most medications, beta-blockers are metabolized predominately in the liver(both the active and inactive compounds). Approximately a quarter of the ingested drug reaches systemic circulation due to the first-pass metabolism in the hepatic circulation.

The active metabolite of propranolol is 4-hydroxypropranolol, which is formed through hydroxylation using the CYP2D6 enzyme.

Furthermore, like most ingested medications, propranolol is predominantly cleared by the renal system, with a half-life of about 3 to 6 hours in patients with healthy renal systems.

Propranolol administration can be either oral or intravenous. With intravenous administration, there should also be continuous electrocardiogram monitoring with a slow infusion. This route of administration primarily occurs in an inpatient setting.

The doses of propranolol vary, being primarily dependent on what condition the medication is treating.

Adverse Effects

Common side effects of using propranolol include bradycardia, gastrointestinal issues, abdominal pain, nausea, erectile dysfunction, and wheezing/bronchospasms. 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.

Contraindications

Prescribers should exercise extreme caution when prescribing beta-blockers to patients with diabetes. This is because this class of medication can mask the symptoms of hypoglycemia, which includes flushing, tachycardia, sweating, and dizziness.

Furthermore, since the main effect of propranolol is to decrease heart rate, it is contraindicated in those who have bradycardia (less than 60 beats per minute).

Propranolol is also contraindicated in those with any lung pathologies, such as COPD, asthma, or emphysema. The pathophysiology of this mechanism is solely due to the effects that beta-2 receptors have on lung function. Normally, activation of beta-2 receptors vasodilates the smooth muscle in the lungs. When using agents like propranolol in patients with underlying lung issues, the blockage of beta-2 causes vasoconstriction of smooth muscle, worsening respiratory function. Physicians should only prescribe selective beta-blockers in such patients; these drugs only block beta-1 receptors and spare beta-2 receptors.

During cocaine toxicity, prescribers should never use any beta-blocker with an unopposed alpha blockade since this can lead to massive unopposed alpha-adrenergic activity and lead to an enormous spike in blood pressure which may even result in death.

Since propranolol is metabolized by hepatic enzymes and excreted through the renal system, prescribers should proceed with caution when prescribing it to a patient with known hepatic or renal impairments. Furthermore, dosages may need to be adjusted to avoid toxicity resulting from the inability to metabolize or clear the medication from the body properly.

Monitoring

Whenever a patient receives propranolol therapy, it is beneficial to routinely monitor their blood pressure, pulse, and respiratory rate. It is especially important in those with coronary artery disease, COPD, or any other condition that beta-blockade might negatively affect. Regular monitoring is possible at home with portable blood pressure and pulse monitors or routinely scheduled visits to primary care physicians. Physicians should also adjust doses as needed to achieve desired therapeutical outcomes.

Patients receiving propranolol therapy parenterally for conditions such as thyroid storm will need continuous cardiac monitoring in the inpatient setting, typically achieved with the patient connected to constant cardiac monitoring devices.

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.

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. [Level 5]

Review Questions

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References

1.
Kalam MN, Rasool MF, Rehman AU, Ahmed N. Clinical Pharmacokinetics of Propranolol Hydrochloride: A Review. Curr Drug Metab. 2020;21(2):89-105. [PubMed: 32286940]

2.
Srinivasan AV. Propranolol: A 50-Year Historical Perspective. Ann Indian Acad Neurol. 2019 Jan-Mar;22(1):21-26. [PMC free article: PMC6327687] [PubMed: 30692755]

3.
Dézsi CA, Szentes V. The Real Role of β-Blockers in Daily Cardiovascular Therapy. Am J Cardiovasc Drugs. 2017 Oct;17(5):361-373. [PMC free article: PMC5591796] [PubMed: 28357786]

4.
LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. National Institute of Diabetes and Digestive and Kidney Diseases; Bethesda (MD): Jan 15, 2017. Propranolol. [PMC free article: PMC547852] [PubMed: 31643543]

5.
Martin K, Blei F, Chamlin SL, Chiu YE, Frieden IJ, Frommelt PC, Garzon MC, Kwon EK, MacLellan-Tobert S, Mancini AJ, Seefeldt M, Sidbury R, Siegel DH, Drolet BA, Boucek RJ. Propranolol treatment of infantile hemangiomas: anticipatory guidance for parents and caretakers. Pediatr Dermatol. 2013 Jan-Feb;30(1):155-9. [PMC free article: PMC4786439] [PubMed: 23316721]

6.
Steenen SA, van Wijk AJ, van der Heijden GJ, van Westrhenen R, de Lange J, de Jongh A. Propranolol for the treatment of anxiety disorders: Systematic review and meta-analysis. J Psychopharmacol. 2016 Feb;30(2):128-39. [PMC free article: PMC4724794] [PubMed: 26487439]

7.
Rehsia NS, Dhalla NS. Mechanisms of the beneficial effects of beta-adrenoceptor antagonists in congestive heart failure. Exp Clin Cardiol. 2010 Winter;15(4):e86-95. [PMC free article: PMC3016066] [PubMed: 21264074]

8.
Wang DW, Mistry AM, Kahlig KM, Kearney JA, Xiang J, George AL. Propranolol blocks cardiac and neuronal voltage-gated sodium channels. Front Pharmacol. 2010;1:144. [PMC free article: PMC3153018] [PubMed: 21833183]

9.
Metra M, Nodari S, Dei Cas L. Beta-blockade in heart failure: selective versus nonselective agents. Am J Cardiovasc Drugs. 2001;1(1):3-14. [PubMed: 14728047]

10.

Shin J, Johnson JA. Pharmacogenetics of beta-blockers. Pharmacotherapy. 2007 Jun;27(6):874-87. [PMC free article: PMC2735790] [PubMed: 17542770]

11.
Ripley TL, Saseen JJ. β-blockers: a review of their pharmacological and physiological diversity in hypertension. Ann Pharmacother. 2014 Jun;48(6):723-33. [PubMed: 24687542]

12.
Farzam K, Jan A. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Aug 22, 2023. Beta Blockers. [PubMed: 30422501]

13.
Ji Y, Chen S, Wang Q, Xiang B, Xu Z, Zhong L, Yang K, Lu G, Qiu L. Intolerable side effects during propranolol therapy for infantile hemangioma: frequency, risk factors and management. Sci Rep. 2018 Mar 09;8(1):4264. [PMC free article: PMC5844887] [PubMed: 29523832]

14.
Pozzi R. [True and presumed contraindications of beta blockers. Peripheral vascular disease, diabetes mellitus, chronic bronchopneumopathy]. Ital Heart J Suppl. 2000 Aug;1(8):1031-7. [PubMed: 10993010]

15.
Tucker WD, Sankar P, Theetha Kariyanna P. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jan 30, 2023. Selective Beta-1 Blockers. [PubMed: 29763157]

16.
Sen A, Fairbairn T, Levy F. Best evidence topic report. Beta-Blockers in cocaine induced acute coronary syndrome. Emerg Med J. 2006 May;23(5):401-2. [PMC free article: PMC2564096] [PubMed: 16627850]

17.
Akbar S, Alorainy MS. The current status of beta blockers' use in the management of hypertension. Saudi Med J. 2014 Nov;35(11):1307-17. [PMC free article: PMC4362137] [PubMed: 25399206]

18.
Peterson CD, Leeder JS, Sterner S. Glucagon therapy for beta-blocker overdose. Drug Intell Clin Pharm. 1984 May;18(5):394-8. [PubMed: 6144498]

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