DIPLAR

Propranolol 10/20

GENERIC NAME: Propranolol Hydrochloride

PHARMACOLOGICAL CLASS: Beta-blocker (Non-selective)

THERAPEUTIC CATEGORY: Antihypertensive

COMPOSITION AND PRESENTATION:

DIPLAR 10

Compostion:
Each tablet contains Propranolol Hydrochloride 10 mg
Presentation:
30 tablets X 5 blisters

DIPLAR 20

Composition:
Each tablet contains Propranolol Hydrochloride 20 mg.
Presentation:
30 tablets X 5 blisters

MOLECULAR INTRODUCTION

Propranolol is a non-selective beta-adrenergic receptor blocking agent. It has no other autonomic nervous system activity. Propranolol is a competitive antagonist which specifically competes with beta-adrenergic receptor stimulating agents for available beta-receptor sites. When access to beta-adrenergic receptor sites is blocked by propranolol, the chronotropic, inotropic and vasodilator responses to beta-adrenergic stimulation are decreased proportionately.

Beta-adrenergic blockade is useful in some clinical conditions in which sympathetic activity is excessive or inappropriate, and therefore, detrimental to the patient. Sympathetic stimulation is however, vital in some situations (e.g. in patients with AV block or with a severely damaged heart) and should be preserved. The basic objective of beta-adrenergic blockade is to decrease adverse sympathetic stimulation but not to the degree that impairs necessary sympathetic support. Beta-blockade results in bronchial constriction by interfering with endogenously or exogenously induced bronchodilation.

MECHANISM OF ACTION:

Propranolol is a non-selective beta blocker, i.e. it blocks the action of epinephrine and norepinephrine on both β1- and β2-adrenergic receptors. It has little intrinsic sympathomimetic activity (ISA) but has strong membrane stabilizing activity (only at high blood concentrations, e.g. overdosage). Research has also shown that Propranolol has inhibitory effects on the norepinephrine transporter and/or stimulates norepinephrine release (present experiments have

shown that the concentration of norepinephrine is increased in the synapse but do not have the ability to discern which effect is taking place). Since Propranolol blocks β-adrenoceptors, the increase in synaptic norepinephrine only results in α-adrenergic activation, with the α1-adrenoceptor being particularly important for effects observed in animal models. Therefore, some have suggested that it be looked upon as an indirect α1 agonist as well as a β antagonist.

INDICATION & DOSAGE

HYPERTENSION

It is usually used in combination with other drugs, particularly a thiazide diuretic. Propranolol can, however, in certain patients, be used alone or as an initial agent in patients in whom, in the judgment of the physician, treatment should be started with a beta-blocker rather than a diuretic. It has been suggested, but not established, that propranolol may achieve a better antihypertensive effect in patients with normal or elevated plasma renin activity (PRA) than those with low PRA. Propranolol by itself is not recommended for the emergency treatment of hypertensive crisis. It is, however, sometimes used as an adjunct to counteract the unwanted effect (tachycardia) of the primary agents used in these situations

In the treatment of hypertension, propranolol may be started by administering the drug in 2 equal daily doses of 40 mg. This may be increased, if necessary, in one week, to 80 mg twice daily, before breakfast and at bedtime.

ANGINA PECTORIS (prophylaxis)

Propranolol may reduce the oxygen requirement of the heart at any level of effort by blocking catecholamine induced increases in the heart rate, systolic blood pressure, and the velocity and extent of myocardial contraction.

Therapy may be initiated with 20 to 40 mg twice daily before meals. If satisfactory response is not obtained after 1 week, dosage should be increased to 80 mg twice daily.

POST MYOCARDIAL INFARACTION

For the reduction of cardiovascular mortality in patients who have survived the acute phase of a myocardial infarction and who are clinically stable. In the study which showed this benefit, treatment with propranolol began between 5 and 21 days after the acute phase.

Therapy may be initiated with a 20 mg dose. If no adverse reaction is noted, dose may be increased to 40 mg three times daily.

PROPHYLAXIS OF MIGRAINE

Normally used as prophylaxis of migraine headache. However, it is not indicated for the treatment of acute migraine attacks. The antimigraine effect may be due to inhibition of vasodilatation or arteriolar spasms over the cortex. Beta-adrenergic receptors have been demonstrated in the pial vessels of the brain.

Dosage must be individualized. The initial dose is 40 mg twice daily. The dose may then be gradually increased until optimum migraine prophylaxis is achieved. The usual effective dose range is 80 to 160 mg/day.

HYPERTROPHIC SUBAORTIC STENOSIS

The management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress induced angina, palpitations, and syncope. Propranolol may also improve exercise performance. The effectiveness of propranolol in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-adrenergic receptor stimulation. Clinical improvement may be temporary.

Dose: 20 to 40 mg, 3 or 4 times daily, before meals and at bedtime.

PHEOCHROMOCYTOMA:

After primary treatment with an alpha-adrenergic blocking agent has been instituted, propranolol may be useful as adjunctive therapy if the control of tachycardia becomes necessary before or during surgery.

Preoperatively: 60 mg daily, in divided doses, for 3 days before surgery, concomitantly with an alpha-receptor blocking agent.

Malignant cases: 30 mg daily, in divided doses.

TACHYARRYTHMIAS

If digitalis induced tachyarrhythmias persist following discontinuance of digitalis and correction of electrolyte abnormalities, they may be reversible with oral propranolol.

Dose: 10 to 30 mg 3 or 4 times daily, before meals and at bedtime.

ESSENTIAL TREMORS:

Useful for the management of essential tremor. The antitremor effects may be exerted through both peripheral and central sites of action. Doses must be individualized. The initial dose is 80 mg daily in divided doses. The dosage may be increased to 120 to 160 mg daily for optimal effects. If a patient does not respond to the drug within this dosage range, it is unlikely that further increases in dosage will produce a therapeutic effect, although a few patients have benefited from a daily dose of 240 mg. In elderly patients, doses above 120 mg daily may increase the risk of side effects such as bradycardia, syncope and bronchospasm.

PHARMACOKINETICS

Absorption:

Complete absorption after oral administration**.** A large part of the absorbed drug is lost from the systemic circulation due to first-pass metabolism in the liver

Distribution:

Widely distributed into body tissues, including lungs, liver, kidneys and heart .A portion of orally administered dose immediately bound by liver.

Plasma Protein Binding: >90% over a wide range of blood concentrations.

Metabolism:
About 73 percent drug undergoes persystemic hepatic metabolism.

Excretion:
Renal excretion accounts for >90 % and plasma half life is 3-6 hr.

ADVERSE EFFECT:

Gastrointestinal: Nausea, vomiting, epigastric distress, anorexia, bloating, mild diarrhea, constipation.
Dermatologic: A few cases of erythematous rashes.
Others: tinnitus, fever combined with aching and sore throat, flushing of the face.

CONTRAINDICATIONS:

- Bronchospasm, including bronchial asthma;
- allergic rhinitis during the pollen season;
- sinus bradycardia and greater than first degree block;
- cardiogenic shock;
- right ventricular failure secondary to pulmonary hypertension;
- congestive heart failure unless the failure is secondary to a tachyarrhythmia treatable with propranolol

For further information, please contact:
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