PROPEROL
PROPRANOLOL HCl INJECTION BP 1MG/ML

COMPOSITION:

Each ml contains Propranolol Hydrochloride of 1mg and water for injection of q.s.

DOSAGE FORM

Parenteral: Injection, Liquid

PRODUCT DESCRIPTION

A clear colourless solution filled in 1ml clear transparent ampoule with blue band. one such ampoules in a tray and one such tray in a carton with a leaflet. Later, 10 just boxes later packed in a bigger carton.

PHARMACODYNAMICS

Propranolol HCl is a nonselective beta-adrenergic receptor blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by Propranolol HCl, the chronotropic, inotropic, and vasodilator responses to beta-adrenergic stimulation are decreased proportionately. Propranolol is almost completely absorbed from the gastrointestinal tract, but a portion is immediately bound by the liver. Peak effect occurs in one to one-and-one-half hours. The biologic half-life is approximately four hours. There is no simple correlation between dose or plasma level and therapeutic effect, and the dose sensitivity range as observed in clinical practice is wide. The mechanism of the antihypertensive effect of Propranolol HCl has not been established. Among the factors that may be involved in contributing to the antihypertensive action are (1) decreased cardiac output, (2) inhibition of renin release by the kidneys, and (3) diminution of tonic sympathetic nerve outflow from vasomotor centres in the brain. Propranolol HCl has been shown to cause a small increase in serum potassium concentration when used in the treatment of hypertensive patients. In angina pectoris, propranolol generally reduces the oxygen requirement of the heart at any given level of effort by blocking the catecholamine-induced increases in the heart rate, systolic blood pressure, and the velocity and extent of myocardial contraction. Propranolol may increase oxygen requirements by increasing left ventricular fibre length, end diastolic pressure, and systolic ejection period. Propranolol exerts its antiarrhythmic effects in concentrations associated with beta-adrenergic blockade, and this appears to be its principal antiarrhythmic mechanism of action.

PHARMACOKINETICS

Following intravenous administration, the plasma half-life of propranolol is about 2 hours and the ratio of metabolites to parent drug in the blood is lower than after oral administration. In particular 4- hydroxy propranolol is not present after intravenous administration. Propranolol is completely absorbed after oral administration and peak plasma concentrations occur 1 to 2 hours after dosing in fasting patients. The liver removes up to 90% of an oral dose with an elimination half-life of 3 to 6 hours. Propranolol is widely and rapidly distributed throughout the body with highest levels occurring in the lungs, liver, kidney, brain and heart. Propranolol is highly protein bound (80 to 95%).

INDICATION

The emergency treatment of cardiac dysrhythmias and thyrotoxic crisis.

RECOMMENDED DOSE

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The initial dose of PROPEROL is 1 mg (1 mL) injected over one minute. This may be repeated at two-minute intervals until a response is observed or to a maximum dose of 10 mg in conscious patients or 5 mg in patients under anaesthesia.

Elderly
Evidence concerning the relation between blood level and age is conflicting. With regard to the elderly, the optimum dose should be individually determined according to clinical response.

Children
Dosage should be individually determined and the following is only a guide. 0.025 to 0.05 mg/kg injected slowly under ECG control and repeated three or four times daily as required.

ROUTE OF ADMINISTRATION

Intravenous

CONTRAINDICATION

Propranolol HCl is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure unless the failure is secondary to a tachyarrhythmia treatable with Propranolol HCl.

WARNING AND PRECAUTIONS

WARNINGS

Hypersensitivity reactions, including anaphylactic/anaphylactoid reactions, have been associated with the administration of propranolol.

Cardiac Failure: Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure.

In Patients without a History of Heart Failure: Continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or Propranolol HCl should be discontinued (gradually, if possible).

In Patients With Angina Pectoris: There have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of Propranolol HCl therapy.

Nonallergic Bronchospasm: (e.g. chronic bronchitis, emphysema) Propranolol HCl should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

Major Surgery: Propranolol HCl, like other beta blockers, is a competitive inhibitor of beta-receptor agonists, and its effects can be reversed by administration of such agents, (e.g., dobutamine or isoproterenol).

Diabetes and Hypoglycaemia: Hypoglycaemic attacks may be accompanied by a precipitous elevation of blood pressure in patients on propranolol.

Acute increases in blood pressure have occurred after insulin-induced hypoglycaemia in patients on propranolol.

Thyrotoxicosis: Propranolol may change thyroid-function tests, increasing T4 and reverse T3 and decreasing T3.

In Patients with Wolf-Parkinson-White Syndrome: Several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. Skin Reactions: Cutaneous reactions, including Stevens-Johnson Syndrome, toxic epidermal necrolysis, exfoliative dermatitis, erythema multiforme, and urticaria, have been reported with use of propranolol.

PRECAUTIONS

General Propranolol should be used with caution in patients with impaired hepatic or renal function. Propranolol HCl is not indicated for the treatment of hypertensive emergencies.

Patients should be told that Propranolol HCl may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

INTERACTIONS WITH OTHER MEDICAMENTS

PROPEROL modifies the tachycardia of hypoglycaemia. Caution must be exercised in the concurrent use of PROPEROL and hypoglycaemic therapy in diabetic patients. PROPEROL may prolong the hypoglycaemic response to insulin.

Care must be exercised in prescribing a beta-adrenoreceptor blocking medicine with Class I antidysrhythmic agents such as disopyramide.

Digitalis glycosides in association with beta-adrenoreceptor blocking medicines may increase atrioventricular conduction time.

Combined use of beta-adrenoreceptor blocking medicines and calcium channel blockers with negative inotropic effects (e.g. verapamil, diltiazem) can lead to an exaggeration of these effects particularly in patients with impaired ventricular function and/or SA or AV conduction abnormalities. This may result in severe hypotension, bradycardia and cardiac failure. Neither

the beta-adrenoreceptor blocking medicine nor the calcium channel blocker should be administered intravenously within 48 hours of discontinuing the other.

Concomitant therapy with dihydropyridines e.g. nifedipine, may increase the risk of hypotension, and cardiac failure may occur in patients with latent cardiac insufficiency.
Concomitant use of sympathomimetic agents e.g. adrenaline, may counteract the effect of beta adrenoreceptor blocking medicines. Caution must be exercised in the parenteral administration of preparations containing adrenaline to patients taking beta-adrenoreceptor blocking medicines as, in rare cases, vasoconstriction, hypertension and bradycardia may result.

Administration of propranolol during infusion of lignocaine may increase the plasma concentration of lignocaine by about 30%. Patients already receiving propranolol tend to have higher lignocaine levels than controls. The combination should be avoided.

Concomitant use of cimetidine or hydralazine will increase, whereas concomitant use of alcohol will decrease, the plasma levels of propranolol.

Beta-adrenoreceptor blocking medicines may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. If the two medicines are co-administered, the beta-adrenoreceptor blocking medicine should be withdrawn several days before discontinuing clonidine. If replacing clonidine by beta adrenoreceptor blocking medicine therapy, the introduction of beta-adrenoreceptor blocking medicine should be delayed for several days after clonidine administration has stopped.

Caution is necessary if ergotamine, dihydroergotamine or related compounds are given in combination with propranolol since vasospastic reactions have been reported in a few patients.

Concomitant use of prostaglandin synthetase inhibiting medicines e.g. ibuprofen and indomethacin, may decrease the hypotensive effects of propranolol.

Concomitant administration of propranolol and chlorpromazine may result in an increase in plasma levels of both medicines. This may lead to an enhanced antipsychotic effect for chlorpromazine and an increased antihypertensive effect for propranolol.

Pharmacokinetic studies have shown that the following agents may interact with propranolol due to effects on enzyme systems in the liver which metabolise propranolol and these agents: quinidine, propafenone, rifampicin, theophylline, warfarin, thioridazine and dihydropyridine calcium channel blockers such as nifedipine, nisoldipine, nicardipine, isradipine and lacidipine. Owing to the fact that blood concentrations of either agent may be affected dosage adjustments may be needed according to clinical judgement.

PREGNANCY AND LACTATION

Pregnancy

As with all other medicines, PROPEROL should not be given in pregnancy unless its use is essential. There is no evidence of teratogenicity with PROPEROL. However, beta-adrenoreceptor blocking medicines reduce placental perfusion, which may result in intra-uterine foetal death, immature and premature deliveries. In addition, adverse effects (especially hypoglycaemia and bradycardia in the neonate and bradycardia in the foetus) may occur. There is an increased risk of cardiac and pulmonary complications in the neonate in the post-natal period.

Lactation

Most beta-adrenoreceptor blocking medicines, particularly lipophilic compounds, will pass into breast milk although to a variable extent. Breast feeding is therefore not recommended following administration of these compounds.

SIDE EFFECTS

PROPEROL is usually well tolerated. In clinical studies, the undesired events reported are usually attributable to the pharmacological actions of propranolol.

The following undesired events, listed by body system, have been reported:

Cardiovascular: bradycardia; heart failure deterioration; postural hypotension which may be associated with syncope; cold extremities. In susceptible patients: precipitation of heart block; exacerbation of intermittent claudication; Raynaud's phenomenon.

CNS: confusion; dizziness; mood changes; nightmares; psychoses and hallucinations; sleep disturbances.

Endocrine: Hypoglycaemia in neonates, infants, children, elderly patients, patients on haemodialysis, patients on concomitant antidiabetic therapy, patients with prolonged fasting and patients with chronic liver disease has been reported.

Gastrointestinal: gastrointestinal disturbance.

Haematological: purpura; thrombocytopenia.

Integumentary: alopecia; dry eyes; psoriasis form skin reactions; exacerbation of psoriasis; skin rashes.

Neurological: paraesthesia.

Respiratory: bronchospasm may occur in patients with bronchial asthma or a history of asthmatic complaints, sometimes with fatal outcome.

Special senses: visual disturbances.

Others: fatigue and/or lassitude (often transient); an increase in ANA (Antinuclear Antibodies) has been observed, however the clinical relevance of this is not clear.

SYMPTOMS AND TREATMENT OF OVERDOSE

The symptoms of overdosage may include bradycardia, hypotension, acute cardiac insufficiency, and bronchospasm.

General treatment should include close supervision, treatment in an intensive care ward, the use of gastric lavage, activated charcoal and a laxative to prevent absorption of any medicine still present in the gastrointestinal tract, the use of plasma or plasma substitutes to treat hypotension and shock.

Excessive bradycardia can be countered with atropine 1 to 2 mg intravenously and/or a cardiac pacemaker. If necessary, this may be followed by a bolus dose of glucagon 10 mg intravenously. If required, this may be repeated or followed by an intravenous infusion of glucagon 1 to 10 mg/hour depending on response. If no response to glucagon occurs or if glucagon is unavailable, a beta adrenoreceptor stimulant such as dobutamine 2.5 to 10 mg/kg/minute by intravenous infusion may be given.

Dobutamine, because of its positive inotropic effect could also be used to treat hypotension and acute cardiac insufficiency. It is likely that these doses would be inadequate to reverse the cardiac effects of beta-adrenoreceptor blockade if a large overdose has been taken. The dose of dobutamine should therefore be increased, if necessary, to achieve the required response according to the clinical condition of the patient.

Bronchospasm can usually be reversed by beta-2 agonist bronchodilators such as salbutamol; large doses may be required, and the dose should be titrated according to the clinical response. Oxygen or artificial ventilation may be required in some cases.

EFFECT ON ABILITY TO DRIVE AND USE MACHINE

NA.

PRECLINICAL SAFETY DATA

NA

INSTRUCTION FOR USE

NA

STORAGE CONDITION’

Store at a temperature below 30^0C & Protect from light.

SHELF LIFE

36 Months. 'Single Use', 'Discard the unused portion’.

PRESENTATIONS

The 1ml ampoule was packed in a tray and placed in the box. Later 10 such boxes were packed in one carton together with package insert.

MANUFACTURED BY:
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PRODUCT REGISTRATION HOLDER:
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