Labetalol

Labetalol (trade names Normodyne and Trandate) is a mixed alpha/beta adrenergic antagonist that is used to treat high blood pressure.

Labetalol acts by blocking alpha and beta adrenergic receptors, resulting in decreased peripheral vascular resistance without significant alteration of heart rate or cardiac output. The β:α antagonism of labetalol is approximately 3:1.

Blocks α1 selective, β non-selective (potency < propranolol). ICP reduces or no change. Pulse rate: decreases or no change. The cardiac output does not change. It does not exacerbate coronary ischemia. May be used in controlled CHF, but not in overt CHF. Contraindicated in asthma. Renal failure: same dose. Side effects: fatigue, dizziness, orthostatic hypotension.

ICP reduces or no change [1)].

Labetalol combines both selective, competitive, alpha-1-adrenergic blocking and nonselective, competitive, beta-adrenergic blocking activity in a single substance. In man, the ratios of alpha- to beta- blockade have been estimated to be approximately 1:3 and 1:7 following oral and intravenous (IV) administration, respectively. The principal physiologic action of labetalol is to competitively block adrenergic stimulation of β-receptors within the myocardium (β1-receptors) and within bronchial and vascular smooth muscle (β2-receptors), and α1-receptors within vascular smooth muscle. This causes a decrease in systemic arterial blood pressure and systemic vascular resistance without a substantial reduction in resting heart rate, cardiac output, or stroke volume, apparently because of its combined α- and β-adrenergic blocking activity.

It has a particular indication in the treatment of pregnancy-induced hypertension which is commonly associated with pre-eclampsia.

It is also used to treat chronic and acute hypertension of pheochromocytoma and hypertensive crisis.

For adrenergic agents, when the substituent on the amine nitrogen is greater in size than a t-butyl group, then the molecule typically is found to have receptor affinity without intrinsic activity, and is therefore an antagonist.

Labetalol has two chiral carbons and consequently exists as four stereoisomers.

Two of these isomers, the (S,S)- and (R,S)- forms are inactive. The third, the (S,R)-isomer, is a powerful α1 blocker. The fourth isomer, the (R,R)-isomer which is also known as dilevalol, is a mixed nonselective β blocker and selective α1 blocker.

Labetalol has local anesthetic activity.

Labetalol, in animal models, was found to cross the blood-brain-barrier in only negligible amounts.

Oral (PO)

Undergoes first-pass liver degradation, therefore requires higher doses PO. PO onset: 2 hrs, peak: 4 hrs. ℞ PO: To convert IV → PO, start with 200 mg PO BID. To start with PO, give 100 mg BID, and increase 100 mg/dose q 2 day; max. = 2400 mg/day.

Intravenous (IV)

Onset 5 mins, peak 10 mins, duration 3–6 hrs. ℞ IV: patient supine; check BP q 5 min; give each dose slow IVP (over 2 min) q 10 minutes until desired BP achieved; dose sequence: 20, 40, 80, 80, then 80 mg (300 mg total). Once controlled, use ≈ same total dose IVP q 8 hrs. ℞ IV drip (alternative): add 40 ml (200 mg) to 160 ml of IVF (result: 1 mg/ml); run at 2 ml/min (2 mg/min) until desired BP (usual effective dose = 50–200 mg) or until 300 mg given; then titrate rate (bradycardia limits dose, increase slowly since effect takes 10–20 minutes).

Fifteen patients who had undergone neurovascular surgery for arteriovenous malformations or cerebrovascular aneurysms and had intracranial pressure (ICP) monitors were studied. The patients had been treated initially with sodium nitroprusside to maintain their arterial BP in a prescribed range, but, because of excessive nitroprusside dose requirements, they were considered either to have refractory BP or to be at risk for thiocyanate toxicity. Intravenous labetalol therapy was started either by frequent bolus pulse therapy every 1 to 2 h or by continuous infusion therapy. The degree of desired arterial BP control and the effects on ICP and cerebral perfusion pressure (CPP) were assessed and compared with the results during nitroprusside therapy. The degree of arterial BP control with labetalol was assessed to be good; 11 patients were weaned off nitroprusside and the remaining four patients had a substantial reduction in their nitroprusside requirements, needing an average of only 1.5 micrograms/kg.min of nitroprusside to control their BP compared with average requirements of 10 micrograms/kg.min of nitroprusside before labetalol therapy. Labetalol therapy improved CPP in six patients and ICP in five patients, with no significant change in cerebral pressure in the remainder. Overall, the CPP in the 15 patients improved from 63 +/- 15 (SD) mm Hg with nitroprusside to 65 +/- 10 mm Hg with labetalol therapy and the ICP decreased from 11.3 +/- 6.1 mm Hg with nitroprusside to 8.6 +/- 3.1 mm Hg with labetalol therapy (p less than .05 by Wilcoxon matched pairs) [2)].

Side effects

Drowsiness

Fatigue

Weakness

Difficulty sleeping

Diminished sexual function

Orthostatic hypotension (due to alpha receptor blockade)

Scalp tingling

Hyperkalemia

Hepatotoxicity

Drug eruption similar to lichen planus

A rare but potentially lethal side effect is respiratory distress.

Labetalol has relative contraindications for use in patients with asthma, congestive heart failure, any degree of heart block, bradycardia, hypotension or those in cardiogenic shock.

[1)] , [2)]

Orlowski JP, Shiesley D, Vidt DG, Barnett GH, Little JR. Labetalol to control blood pressure after cerebrovascular surgery. Crit Care Med. 1988 Aug;16(8):765-8. PubMed PMID: 3396371.