# Propranolol

## Adverse Effects

### Cardiovascular

Use of a nonselective beta-blocker like propranolol may at least blunt cardiac output in some patients, especially those with preexisting left ventricular systolic dysfunction and during exertion. Data have shown that cardiac conditioning can delay or attenuate this side effect of propranolol.

Abrupt cessation of propranolol therapy may result in hypertension, myocardial infarction, and angina pectoris in some patients.

Paradoxical hypertension may occur in patients with pheochromocytoma, unless alpha-adrenergic blockade is already instituted.

At least two cases of electrical alternans associated with propranolol are reported from pediatric cases. In one case, electrical alternans was clearly not rate-related (since it occurred during propranolol therapy at a slower rate than the patient's “native” ventricular tachycardia) and was associated with echocardiographically-demonstrated mechanical alternans.

Common (1% to 10%): Hypotension, cold extremities, Raynaud's phenomenon Uncommon (0.1% to 1%): Heart failure, precipitation of heart block Rare (less than 0.1%): Exacerbation of claudication, postural hypotension (which may be associated with syncope) Frequency not reported: Bradycardia, congestive heart failure[Ref]

### Nervous system

Rare cases of paresthesias and myasthenia gravis have been associated with propranolol.[Ref]

Common (1% to 10%): Fatigue and/or lassitude (often transient), sleep disturbances, nightmares, sleep disorder, agitation, somnolence, irritability Rare (less than 0.1%): Dizziness, paresthesia (especially of the hands) Very rare (less than 0.01%): Seizure (linked to hypoglycemia) Frequency not reported: Reduction or loss of libido, lightheadedness, mental depression (manifested by insomnia), weakness, catatonia, hallucinations, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium

## Renal

There are reports of patients who experienced reversible renal insufficiency with no decline in systemic blood pressure, but these patients had preexisting renal disease. This may be important in patients with preexisting renal insufficiency. New or worsened renal dysfunction has been reported in patients with underlying renal disease and no decline in systemic blood pressure.

Uncommon (0.1% to 1%): Renal insufficiency (related to lowering of systemic blood pressure)[Ref]

## Respiratory

Rare (less than 0.1%): Dyspnea, worsening of reactive airways diseases, bronchospasm in patients with bronchial asthma or a history of asthmatic complaints (sometimes fatal)

Limited data have shown a mean fall in maximal midexpiratory flow rate (MMFR) during propranolol therapy relative to placebo in nine of ten patients whose lung function was assessed. Interestingly, the fall was not related to smoking or to atopic status, suggestive of resting beta-adrenergic bronchodilator activity in nonasthmatic subjects.

Non-selective beta-blockers, such as propranolol, are used with caution in patients with asthma and chronic obstructive pulmonary disease due to inhibition of bronchodilation.

## Endocrine

Beta-blockers, such as propranolol, are used with caution in patients with diabetes due to masking of the catecholamine response to hypoglycemia. Propranolol may also mask the signs of hyperthyroidism by the same mechanism.

Propranolol has been associated with significant increases in serum triglycerides, fasting blood glucose, and LDL and VLDL cholesterol, and significant decreases in HDL cholesterol.

Very rare (less than 0.01%): Hypoglycemia (particularly in neonates, infants, children, elderly patients, patients on hemodialysis, patients on concomitant antidiabetic therapy, patients with prolonged fasting and patients with chronic liver disease), hypertriglyceridemia

## Gastrointestinal

Uncommon (0.1% to 1%): Anorexia, nausea, vomiting, diarrhea, abdominal pain, flatulence, decreased appetite

## Psychiatric

One study of 34 hypertensive patients who were taking propranolol found the incidence of depressive symptoms in this population to be 50% to 74% (depending on the criteria used). Propranolol-induced depression may be more likely in patients with a personal or family history of depression. Of the 34 patients, 12 had a history of depression and 8 had a history of substance abuse, alcoholism, or a family history of psychiatric disorders. Since none of the 12 patients with a history of depression were clinically depressed at the start of propranolol therapy and were comparable by age, diagnosis, and propranolol dosage to the other 22 patients, a comparison was made. Patients with a personal or family history of depression had significantly higher scores on depression scales than those without such histories.

A 72-year-old retired college professor with no history of affective disorders developed progressive sadness, tearfulness, hopelessness, decreased energy, social withdrawal, anhedonia, insomnia, and decreased memory and concentration within two weeks after beginning propranolol monotherapy for hypertension. The signs and symptoms of depression resolved upon substitution with a thiazide diuretic. Interestingly, the patient later was treated for recurrent depression while not receiving propranolol.

Rare cases of psychoses associated with propranolol have been reported.

Rare (less than 0.1%): Depression (dose dependent), hallucinations, psychoses, mood changes, confusion, memory loss[Ref]

## Hypersensitivity

Rare (less than 0.1%): Anaphylaxis, contact dermatitis

## Hematologic

Uncommon (0.1% to 1%): Reduction of platelet adhesiveness, thrombocytopenic purpura, nonthrombocytopenic purpura, agranulocytosis, eosinophilia

## Dermatologic

Rare (less than 0.1%): Psoriatic flares Frequency not reported: Stevens - Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, erythema multiforme, urticaria, purpura, alopecia, skin rashes, SLE-like reactions

## Immunologic

Postmarketing reports: Enhanced immune system

Propranolol can enhance the immune system by causing an increase in the number of circulating T cells, increased interleukin-2 (IL-2) secretion, increased expression of IL-2 receptors, and increased lymphocyte production in response to the T cell mitogen Con A. Interestingly, NK (natural killer) cell activity may be decreased during propranolol therapy, although the number of circulating NK cells may remain unchanged. These results are consistent with previous data showing decreased immunologic function during periods of elevated sympathetic activity, such as congestive heart failure, uremia, or life-threatening events.

### Genitourinary

Frequency not reported: Male impotence, Peyronie's disease

### Metabolic

Frequency not reported: Weight gain[Ref]

The mechanism by which propranolol induces weight gain is unknown. Some investigators have reported a 4% to 9% reduction in total energy expenditure and a 25% reduction in thermogenic response to food during beta-blocker treatment.

### Musculoskeletal

Very rare (less than 0.01%): Myasthenia gravis like syndrome or exacerbation of myasthenia gravis Frequency not reported: Myopathy, myotonia

### Hepatic

Very rare (less than 0.01%): Elevated liver function tests[Ref]

### Ocular

Rare (less than 0.1%): Dry eyes, visual disturbances

## Pregnancy and Breastfeeding Warnings

- US FDA pregnancy category C

    - Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant.
    - Beta blockers may cause decreased placental perfusion, fetal and neonatal bradycardia, and hypoglycemia. Propranolol has been used safely to treat a variety of conditions during pregnancy, including hypertension and pheochromocytoma in the mother, and tachyarrhythmias in both the mother and fetus. There are a number of abnormalities associated with the use of propranolol during pregnancy, but many of these may be attributable to underlying diseases. These abnormalities include some signs of beta-blockade, such as bradycardia, hypoglycemia, and respiratory depression. Other abnormalities that may be due to propranolol include intrauterine growth retardation, small placentas, polycythemia, thrombocytopenia, and hypocalcemia

- Excreted into human milk
    - Some recommend monitoring infant for signs and symptoms of beta-brocade and schedule feeds at least 3 hours after maternal propranolol administration

# References

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