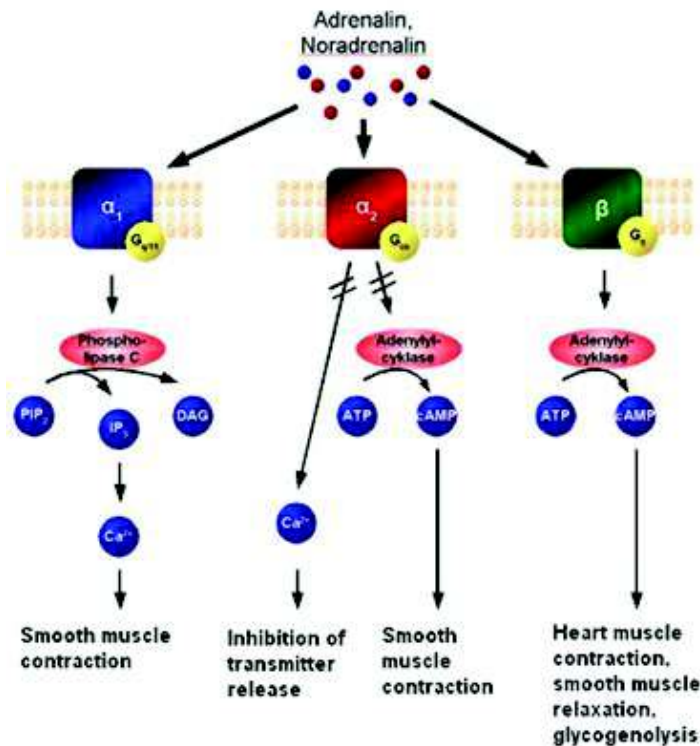


Propranolol

Old drug with many uses

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James W Black discovered propranolol (first drug in its class – beta (β) blocker) in 1960s and was awarded the Nobel Prize in Medicine for this in 1988. It is on the World Health organisation list of essential medicines. Propranolol is a non selective β_1 and β_2 adrenergic and noradrenergic blocker.

Beta (β) cells are present in the heart causing heart muscle contraction, also smooth muscle relaxation in other parts of the body as well an effect on glycogenolysis which affects blood sugar levels. There are three types of β cells, β_1 which affects the heart rate and the AV node conduction of the heart and β_2 which are responsible for smooth muscle relaxation such as bronchodilation (best known one specific for β_2 agonist/bronchodilator is salbutamol (Ventolin®) and β_3 are involved in breakdown of lipids and conversion of triglycerides to glycerol.

Some of the recognised uses for propranolol include treatment of hypertension, angina, tachyarrhythmias (fast irregular heart rate), myocardial infarction (heart attack), racing heart beat and tremor associated with hyperthyroidism, anxiety and lithium therapy, essential tremor (adverse effect of numerous medications), rhythmic shaking about 4-12 cycles per minute (Hz), migraine and cluster headache

prevention, excessive sweating, infantile haemangiomas, glaucoma, PTSD, akathisia, aggressive behaviours associated with brain injury and thyrotoxicosis.

Why is it used in mental health?

Propranolol is used in a variety of mental health conditions but usually when the first line therapy has not been successful. Most of the conditions where it is used it is for an unlicensed indication – the evidence for use may not be extensive.

Propranolol is used to correct the essential tremor (rhythmic shaking about 4-12 cycles per minute (Hz)) for those taking lithium and other medications where the tremor is causing distress. Propranolol is thus also used for restlessness (akathisia) also associated with adverse effects of medication usually antipsychotics. These indications would be targeting the component that causes smooth muscle relaxation and antagonism of the peripheral β_2 receptors. Targeting the β_1 receptors, may theoretically prevent fear conditioning and reconsolidation of fear associated with PTSD. Thus propranolol has been shown to be successful in some for treatment of PTSD and anxiety. It is commonly used amongst performers for performance anxiety as a one off dose prior to the performance. There are reports that early administration may help with the intrusive thoughts and reduce the severity of later symptoms in PTSD. As propranolol works on the adrenergic system which controls the flight fight mechanisms of the body it has shown some success in patients exhibiting violence or aggression.

Why use in the developmental disability setting?

Propranolol may be effective in controlling rage, irritability and aggression, in ASD and ADHD. Controlling aggression associated with organic brain dysfunction as there is good evidence to show efficacy for the management of agitation and aggression in patients with acquired brain injury.

Often, antipsychotics or D_2 antagonists such as risperidone are used to treat challenging behaviours especially in the context of autistic spectrum disorder. One of the adverse effects of risperidone and some of the older antipsychotics is extrapyramidal side effects including involuntary movements and muscle spasms and propranolol has been prescribed.

Beta blockers have membrane stabilising effect and GABA-mimetic activity; as well as presynaptic $5HT_{1A}$ antagonists.

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These characteristics are what is needed for a good anxiolytic, thus is used second or third line for anxiety symptoms.

What should I be looking at for adverse effects or side effects?

Propranolol causes adverse effects by blocking the adrenergic receptors which will cause dizziness, bradycardia (slowing of heart beat) and hypotension (low blood pressure) and minor effects on other receptors.

Propranolol and other beta blockers can inhibit the effect of melatonin on the body thus causing insomnia and other sleep disturbances. If affecting sleep, propranolol should be taken during the daylight hours to ensure there is no effect on the body's natural melatonin levels. It has been known to be used successfully with patients with Smith Magenis Syndrome where there is an inverted melatonin circadian cycle.

Propranolol's effect on smooth muscles can inhibit bronchodilation and can also precipitate asthma and being an antagonist for beta receptors should not be used for patients with asthma and especially counters the effect of salbutamol and the other beta agonists used to treat asthma symptoms. In these situations, a cardio selective beta blocker such as metoprolol can be used.

Propranolol and the other beta blockers are also associated with fatigue and coldness of the extremities. Some sleep disturbances with nightmares have also been reported. Beta blockers can affect the carbohydrate metabolism causing low or high blood sugar levels in patient who are either have diabetes or not. They can also interfere with metabolic and autonomic responses to hypoglycaemia thereby masking symptoms such as tachycardia (fast heart rate). Weight gain has also been reported. Urinary retention, joint pain, dysuria as well as sexual dysfunction and decreased libido have also been reported.

Other important information about propranolol

Propranolol is also used in the prophylaxis of migraines and in some cases for treatment of anxiety. Propranolol is extensively used in cardiology from the treatment of acute cyanotic episodes in neonates with tetralogy of Fallot and used in heart failure and arrhythmias in the elderly. Beta blockers act principally by attenuating the effects of the sympathetic system on automaticity and conductivity.

Propranolol is also used to control blood pressure so when using it for other indications it is important to monitor the blood pressure to ensure it does not drop too much thus causing dizziness and falls.

When being used for migraine prophylaxis it can begin to work within 2 weeks but may take up to 3 months on stable dose to see the optimal effect. But when used to treat tremor can work within days.

Propranolol has also been used in PTSD acting theoretically by blocking the effects of stress from prior traumatic experiences.

When it is used in context of violence and aggression the mechanism is poorly established but it is assumed to be related to central actions at the β adrenergic and serotonin receptors. This may be through affecting the stress response of the adrenal gland.

Propranolol and other beta blockers have also been reported to exacerbate psoriasis and alopecia and rashes have also been reported.

Propranolol and other beta blockers can blunt the symptoms of hypoglycaemia in diabetics and mask the clinical signs of hyperthyroidism.

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