Module 5.1
β-blockers

Introduction

β blocker medications competitively antagonise the effects of catecholamines at the β receptor, decreasing inotropy and chronotropy. They are commonly prescribed in the management of cardiovascular disease, including heart failure, hypertension, ischaemic heart disease and tachyarrhythmia. Furthermore, they are used to treat migraine, hyperthyroidism and benign tremor. They are uncommonly taken in overdose and can lead to significant morbidity.

Toxicokinetics

The kinetics of β blockers depend on their lipophilicity[1]. Propranolol has the highest lipid solubility, while atenolol has the highest water solubility. High lipid solubility allows propranolol to rapidly cross the blood brain barrier and can result in neurotoxicity. Propranolol also has sodium channel blocking effects which greatly worsens potential toxicity. Similarly, toxicity is increased with sotalol due to its potassium channel blocking effects.[2]

Drug	Receptor	Lipid solubility	½ life (hrs)	Metabolism
Atenolol	β_1	Low	5-9	Renal
Bisoprolol	β_1	Low	9-12	Hepatic/Renal
Carvedilol	β_1 β_2, α_1	Mod	6-10	Hepatic
Labetalol	α_1, β_1 β_2	Mod	4-8	Hepatic
Metoprolol	β_1	Mod	3-4	Hepatic
Propranolol	β_1 β_2	High	3-5	Hepatic
Sotalol	β_1 β_2	Low	9-12	Renal

Pharmacokinetics table adapted from Goldfranks[1]

Risk Assessment

An ECG is crucial in the assessment of β-blocker toxicity. Sinus bradycardia ± 1st degree AV block and interventricular conduction delay are most common dysrhythmia[2]. QRS widening can occur in propranolol toxicity, while QT prolongation and possibly Torsades de Pointes can occur in sotalol poisoning. Other β-blockers, when taken in isolation, are much better tolerated.

In severe poisoning hypotension can occur from bradyarrhythmia as well as direct myocardial depression. Bedside echo can be used to quantify myocardial depression and effectiveness of therapy.

Bronchospasm and respiratory compromise can be precipitated in people with an underlying propensity. Hyperkalaemia and hypo or hyperglycaemia can also be seen[2].

Seizures and coma occur in severe propranolol poisoning due to its ability to cross the blood brain barrier. Ingestions greater than 2g of propranolol are associated with severe toxicity.[3]

It is important to identify any cardioactive co-ingestants, such as calcium channel blockers or TCAs, as this greatly increases potential toxicity[4].

Management

Resuscitation

- Treat hypotension with fluids initially
- Add an adrenaline infusion if hypotension persists despite fluids
- Atropine aliquots can also be considered for bradycardia
- Pacing may be necessary if bradycardia is unresponsive to adrenaline and atropine
- HIET[5] should be commenced if evidence of myocardial depression on bedside echo despite >15mcg/min of adrenaline

Give 1 u/kg bolus of actrapid and commence infusion starting at 100 u/h
Titrate q15min aiming for a MAP > 65, (max 10 units/kg/h)

Give bolus of 50mL 50% glucose and run 50% glucose infusion at 50mL/h,
titrate glucose to achieve euglycaemia

- Coma warrants airway protection
- The role of bicarbonate in propranolol induced sodium channel blockade is controversial due to its questionable effectiveness. If there is evidence of sodium channel blockade on ECG it can be trialled, however if there is no response (narrowing of QRS complexes) following 200mmol, it should be discontinued.
- Torsades de Pointes in sotalol overdose should be treated along standard lines with magnesium, and overdrive pacing if unsuccessful.

Decontamination

- Due to potential toxicity, activated charcoal should be offered to people presenting within 2 hours of immediate release ingestion and 4 hours of a sustained release ingestion. All patients who have required intubation should receive activated charcoal.

Supportive Measures

- Treat seizures along standard lines with titrated benzodiazepines
- Ensure euglycaemia
- Ensure K^+ and Mg^{2+} optimised

Disposition

All cases of β-blocker poisoning should be discussed with the toxicology team and warrant a period of observation with telemetry. Toxicity, should manifest within 6 hours of IR preparations[4]. Severe toxicity requiring inotropes or HIET will require ICU admission.

Additional Information

- Glucagon is not recommended
- Prolonged ACLS should be undertaken if a patient arrests, including consideration of ECMO.

Further reading

- Isbister G and Page C. Chapter 325: Management of β-blocker and calcium channel blocker. Oxford Textbook of Critical Care. 2nd ed. Oxford University Press.

- Graudins A, Min Lee H and Druda D. "Calcium channel antagonist and beta-blocker overdose: antidotes and adjunct therapies." *Br J Clin Pharm* 81(3):452-61

References

1. Nelson L et al. Goldfrank's Toxicologic Emergencies. 9th Ed. 2010. McGrawHill Medical: Sydney.

2. Isbister G and Page C. Chapter 325: Management of β-blocker and calcium channel blocker. Oxford Textbook of Critical Care. 2nd ed. Oxford University Press.

3. eTG Toxicology and Wilderness Medicine: Beta Blockers https://tgldcdp.tg.org.au/viewTopic?topicfile=toxicology-beta-blockers#MPS_d1e368

4. Love J et al. "Acute beta blocker overdose: Factors associated with the development of cardiovascular morbidity." Clin Tox, 2000: 38(3)275-81

5. Kristin M. Engebretsen, Kathleen M. Kaczmarek, Jenifer Morgan & Joel S. Holger (2011) High-dose insulin therapy in beta-blocker and calcium channel-blocker poisoning, Clinical Toxicology, 49:4, 277-283, DOI: 10.3109/15563650.2011.582471