Effects of drugs on heart rate

ASSIGN BUSTER

This investigation tests the effects of various drugs on cardiovascular receptors. The experiment aims to show the differences in heart rate and blood pressure produced from several types of drugs including agonists such as adrenaline, noradrenaline, acetylcholine and their antagonists such as propanolol and atropine. Results are graphed and tabulated and there is a clear trend showing the increase in heart rate and blood pressure with a higher concentration of noradrenaline. It is also shown that in the presence of atropine an antagonist of acetylcholine, the heart rate and blood pressure are significantly affected, showing reduced signs of the effects acetylcholine has on the parasympathetic nervous system.

Introduction:

The aim of the investigation is to test the pharmacological properties of drugs which affect the autonomic nervous system and the cardiovascular system. In this experiment the heart rate and blood pressure from an anaesthetised cat was monitored. The purpose of the tests was to gain experience of in-vivo experimentation and to understand the difficulty in drug, dosage and administration which can have significant effects on the animal if wrongly selected. Drugs used in this experiment were noradrenaline, adrenaline, acetylcholine, propranolol and atropine. Drugs which affect the heart can be categorised into autonomic neurotransmitters, antidysrhythmic drugs and cardiac glycosides/other inotropic drugs. (Rang and Dale)

Noradrenaline is an agonist, which binds to alpha 1+2 and beta 1 adrenoreceptors, which cause vasoconstriction and alters muscle

contractions of the heart (inotropic effects) and alters heart rate by affecting the nerves in the heart, or by changing the rhythm produced by the sinoatrial node (chronotrophic effects). Noradrenaline is a nerve transmitter released by sympathetic nerve terminals. Hypertension, vasoconstriction, tachycardia (or reflex bradycardia), ventricular dysrhythmias

Adrenaline (epinephrine) like noradrenaline stimulates the alpha 1 + 2 and beta 1 receptors as well as beta 2 receptors. It is secreted by the adrenal medulla and is used in treatment of asthma (emergency treatment), anaphylactic shock, cardiac arrest. It may also be added to local anaesthetic solutions

Acetylcholine. Stimulates muscarinic cholinoreceptors and has negative chronotropic and inotrophic effects. Acetylcholine. is released in the following sites: all pre- and post-ganglionic parasympathetic neurons, all preganglionic sympathetic neurons, preganglionic sympathetic fibers (rang and Dale). There are two main classes of acetylcholine receptor. nicotinic acetylcholine receptors and muscarinic acetylcholine receptors. (Rang and Dale).

Atropine is a competitive antagonist for the muscarinic acetylcholine receptor and is referred to as a Atropine Antimuscarinic agents, it can be classified as an anticholinergic drug. Adverse effects of atropine include ventricular fibrillation and Tachycardia.

It belongs to the class II: β-adrenoceptor antagonists. Used in treating sinus bradycardia, that is abnormally low heart rate (< 60 bpm), (Rang and Dale).

Propanolol is a beta adrenoreceptor antagonist. Clinical uses include treating myocardial infarction. Prevents recurrence of tachyarrhythmia provoked by increased sympathetic activity. Propanolol is a β Antagonist (non-selective), which means it can bind to both beta receptors. It is used clinically to treat Angina, hypertension, cardiac dysrhythmias, anxiety tremor, glaucoma; some side effects however include hypoglycaemia and cardiac failure. (Rang and Dale). Propranolol blocks the action of adrenaline and noradrenaline on both β1- and β2-adrenergic receptors.

Different receptor types, the two main α-receptor subtypes, α1 and α2 and three β-adrenoceptor subtypes (β1, β2, β3), all belong to the superfamily of G-protein-coupled receptors. (Rang and Dale)The functions of these receptors include α1-receptors activate phospholipase C, producing inositol trisphosphate and diacylglycerol., α2-receptors inhibit adenylate cyclase, decreasing cAMP formation all types of β-receptor stimulate adenylyl cyclase.

Some of the effects of adrenoreceptors are as follows. α1-receptors cause vasoconstriction, relaxation of gastrointestinal smooth muscle, salivary secretion and hepatic glycogenolysis α2-receptors: inhibition of transmitter release (including noradrenaline and acetylcholine release from autonomic nerves) and contraction of vascular smooth muscle. β1-receptors: increased cardiac rate and force and β2-receptors cause relaxation of visceral smooth muscle, glycogenolysis and muscle tremor. (Rang and Dale).

Method/procedure:

Firstly saline is injected to act as a control to ensure blood rate and pressure remained constant. The following concentrations of saline are used from 1ml/Kg to 5ml/Kg. An electrical stimulus is applied to the vagus (parasympathetic nerves) three times, causing nervous stimulation. An electrical stimulus is then applied to the cardio-accelerator (sympathetic nerves) ensuring accurate testing on the autonomic nervous system. After each test a screen shot of the graphed results are then taken for later reference. Using the software ‘ CardioLab’ the following tests were applied to an anaesthetised cat subject simulation.

Noradrenaline and Adrenaline test:

Different concentrations of 100, 200, 400 and 500ml/kg noradrenaline injected respectively.

Noradrenaline and Acetylcholine test:

1000ml/kg of noradrenaline is injected, followed by 1000ml/kg of acetylcholine.

noradrenaline and propanolol

500ml/kg of noradrenaline is injected followed by 500ml/kg of propanolol. The test is repeated vive-versa.

Acetylcholine and Atropine

The following concentrations of acetylcholine were injected respectively. 50, 75, 90, 100 and 250ml/Kg. 1000ml/Kg of Atropine is added, followed by a

repeat dose of acetylcholine in the following concentrations, 100, 250 and 500ml/Kg.

Results.

(Figures given in tables are based on estimated graph readings.)

Noradrenaline/adrenaline test:

The heart rate and blood pressure increase when noradrenaline is added, there is also slight fluctuation at the peak of the heart rate and blood pressure when the higher dosage of 400ml/kg and 500ml/kg are injected. Noradrenaline works mainly on alpha receptors.

Table 1

Noradrenaline concentration (ml/Kg)	Heart rate peak (bpm)	Blood pressure peak (mm/Hg)
100		
280		
180		
200		
281		
183		

400

285

186

500

285

188

Table 2

Adrenaline concentration (ml/Kg)	Heart rate peak (bpm)	Blood pressure peak (mm/Hg)
100	285	168
200	285	166
400	283	

166

500

283

166

Results show that Low doses of adrenaline mainly affect beta receptors giving a decrease in blood pressure and increased heart rate.

Noradrenaline and acetylcholine test.

The heart rate and blood pressure increase when noradrenaline is given, but as soon as acetylcholine is given the heart rate and blood pressure immediately drop and the animal dies within 5 minutes of acetylcholine being injected blood pressure falling from normal values of 100mg/Hg to 0 and heart rate falling from 180bpm.

Table 3

time (minutes)

Heart rate peak (bpm)

Blood pressure peak (mm/Hg)

0

180

100

1

85

55

2

40

50

3

20

25

4

5

10

5

0

0

Noradrenaline, propanolol

Increase in blood pressure and slight increase in heart rate when noradrenaline is added. Propanolol reduces both blood pressure and heart rate back to a stable rate/pressure. Adding more propanolol has no effect on

the heart rate or blood pressure, however, when a repeat dose of noradrenaline is given the blood pressure and heart rate increase again.

Table 4 shows peak in heart rate/ blood pressure before and after propanolol is added.

Table 4

Before Propanolol is added	After Propanolol is added
Heart rate peak (bpm)	
270	
245	
Blood pressure peak (mm/Hg)	
170	
160	

Acetylcholine and Atropine

From table 5 and graph 7 given, it is shown that there is a rapid decrease in blood pressure and heart rate when acetylcholine is added, blood pressure falling from 90mm/Hg to 15mm/Hg in the first 2 minutes upon administration of 50ml/Kg of acetylcholine. When Atropine is added there is no change to blood pressure and heart rate, however when acetylcholine is injected again the blood pressure and heart rate show a very slight increase.

Table 5 shows Blood pressure and heart rate before atropine is added:

Table 5

concentration of acetylcholine ml/Kg

100

250

Heart rate peak (bpm)

40

20

Blood pressure peak (mm/Hg)

15

18

Table 6 shows Blood pressure and heart rate after atropine is added:

Table 6

concentration of acetylcholine ml/Kg

100

250

Heart rate peak (bpm)

165

165

Blood pressure peak (mm/Hg)

100

110

Discussion:

Adrenaline/noradrenaline.

This experiment demonstrates that low doses of adrenaline mainly affect beta receptors giving a decrease in blood pressure and increased heart rate. The increase in blood pressure is seen due to activation of alpha receptors. As adrenaline is eliminated from the circulation the concentration decreases and the increase in blood pressure is followed by a decrease since adrenaline effects the beta 2 receptors have a higher affinity for adrenaline.

noradrenaline has no effect on beta 2 receptors and thus never causes a decrease in blood pressure. A negative feedback loop can be seen in both cases in which high blood pressure and heart rate causes a decrease in heart rate and thus blood, and vice versa. However with higher doses of adrenaline Adrenal reversal can be seen this means small increase in blood pressure occurs due to competition with noradrenaline. (Rang and Dale 2007)

Adrenaline/ propanolol

Adrenaline causes an increase in blood pressure. At the highest dose beta receptor effects of adrenaline (increased heart rate and decreased blood pressure at the end of the adrenaline effect) are also seen due to the competitive nature of the beta blockade obtained with propranolol. Propranolol is a beta-blocker. It slows down the heart rate and reduces blood pressure. It’s often prescribed for people with high blood pressure

The highest dose beta receptor effects of adrenaline (increased heart rate and decreased blood pressure at the end of the adrenaline effect)

are also seen due to the competitive nature of the beta blockade obtained with propranolol. Propanolol is a non-selective beta-adrenergic receptor blocking agent. It has no other autonomic nervous system activity. Propranolol is a competitive antagonist which specifically competes with β adrenergic receptor stimulating agents for available beta-receptor sites. When access to β adrenergic receptor sites is blocked by propranolol, the chronotropic, inotropic, and vasodilator responses to beta-adrenergic stimulation are decreased. .

Noradrenaline/ acetylcholine

ACH stimulates the parasympathetic system. The Vagus nerve acts on the sino atrial (SA) node of the heart to decrease the heart rate. If too much ACH is given bradychardia can occur. This is shown with the dramatic decrease in blood pressure and heart rate.

Acetylcholine/atropine

A brief explanation of nerve impulses at a synapse, can explain the effect atropine has on acetylcholine. The synapse is the point at which neurons meet. The end of an axon is the region known as a synaptic knob. The synaptic knob contains many vesicles containing neurotransmitters such as acetylcholine and it is sealed by a membrane. The membrane of the cell through which the impulse is being transmitted is called the pre-synaptic membrane while that of the cell to which the signal is to be transferred is

called the post-synaptic membrane. Atropine can be referred to as a neurotoxin and acts by preventing acetylcholine from depolarising the post-synaptic membrane and so prevents generation of the impulse in this cell (www. chm. bris. ac. uk)

Atropine is referred to as an anticholinergic, which blocks the neurotransmitter acetylcholine in the central and the peripheral nervous system

Atropine lowers the activity of all muscles and glands regulated by the parasympathetic nervous system. This occurs because atropine is a competitive antagonist of the muscarinic acetylcholine receptors Acetylcholine reduces the Ca2+ concentration of the intracellular fluid, as shown with the decrease in heart rate and blood pressure from the graphs.