THE ROLE OF PROPRANOLOL HYDROCHLORIDE
(A BETA ADRENERGIC BLOCKER)
IN ANAESTHESIA

By

Mohamed Reda Abdel Gawad

M.B., B.Ch.,D.A.,D.M.

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Faculty of Medicine,

Ain Shams University

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Propranolol hydrochloride (Inderal), issued by I.C.I.

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The Role Of Propranolol Hydrochloride (Inderal) In Anaesthesia

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اسم صاحب الرسالة

محمد رضا احمد عبد الجواد

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INTRODUCTION

INTRODUCTION

Cardiac arrhythmias are sometimes encountered during the course of any surgical procedure performed under anaesthesia and many factors have been invoked as the precipitating cause. Thus pre-operative anxiety, surgical manipulation of the heart, injection of adrenaline, electrolytes imbalance, acid-base changes, hypoxaemia, hypercarbia, hypothermia, acute changes in blood volume and reflex cardiac inhibition or excitation have all been considered of significance.

These factors, whether acting alone or in association with a pre-existing pathological conditions, might easily evoke any type of cardiac arrhythmias.

Cardiac arrhythmias are becoming nowadays more frequent during surgical operations for the following reasons: First, cardiovascular surgery is now undertaken for a wide range of congenital defects and acquired diseases which were previously considered inoperable. Secondly, more older patients are now being operated upon than in the past, due to remarkable increase in life expectancy.

In addition the rapid advances in surgical and anaesthetic techniques have extended the safety of surgery to the point that age is no longer a deterent to surgical therapy.

The group of drugs which are used in the prevention or treatment of cardiac arrhythmias is called the anti-arrhythmia or anti-fibrillatory drugs. This group include the followings :

- Quinidine
- Procaine and procaine amide
- Adrenergic and cholinergic blocking drugs.
- Antihistaminics.
- Some cations such as potassium, magnesium,calcium and barium.

The aim of the present work is to study the effects of **propranolol** "a beta adrenergic blocking agent " on induced arrhythmias in experimental animals and to assess its action on different forms of arrhythmias.

Auricular arrhythmia can be induced by one of the following methods :

i. Topical application of aconitine to an open heart.

ii. Injection of acetylcholine in the substance of the auricle.

iii. Crushing of the auricular muscle.

iv. Topical application of acetylcholine to the region of the sino-atrial node followed by faradic stimulation of the vagus.

Ventricular arrhythmia is induced by :

i. Epinephrine injection in a dog under chloroform or halothane anaesthesia.

ii. Injection of massive doses of cardiac glucosides (Ouabain).

In addition, this study includes the clinical trial of propranolol to evaluate its effects on hyperthyroid reactions occurring during operation on thyroid cases, cardiac irregularities that may develop during halothane anaesthesia, arrhythmias due to surgical manipulation of the heart and finally the role of propranolol, as adjuvent to hypotensive drugs in resistant cases to induced hypotensive anaesthesia.

REVIEW OF THE LITERATURE

REVIEW OF LITERATURE

History of B. adrenergic neurone blocking agents

The concept that effector cells contain excitatory and inhibitory "receptor substances"and that the effects of epinephrine were dependant upon the types of"receptor substances " present was firstly suggested by "Langley"more than sixty years ago.

This hypothesis received support in 1906 when "Dale's comprehensive studies on the adrenergic blocking activities of ergot derivatives were published. Although these drugs completely antagonised and even reversed the excitatory actions of epinephrine, yet they had no effect on the inhibitory actions. The only excitatory action of epinephrine that was not inhibited by ordinary doses of ergot was stimulation of the heart.

These results suggested that the effects of epinephrine were dependant on at least 2 types of receptors, one of which was blocked by the administration of ergot. It remained for "Ahlquist" however in 1948 to define clearly the concept of alpha and beta drenergic receptors that with minor modification is still adhered to-day. This investigator studied the relative potencies of six different

sympathomimetic amines on a variety of effector systems. When the compounds were tested for their abilities to cause vasoconstriction, excitation of the uterus ,contraction of the nictitating membrane, dilatation of the pupil and inhibition of the gut, a constant order of potency emerged.

However, this order of potency was found to be completely reversed when these drugs were tested for their abilities to produce vasodilatation, inhibition of the uterus and myocardial stimulation. Ahlquist postulated that 2 distinct types of adrenergic receptors exist and that the effect of a sympathetic drug on the effector cell depends on the types of receptor with which it is capable of reacting. Receptors having an excitatory effect on stimulation were classified as alpha adrenergic receptors and those with an inhibitory effect of stimulation were classified as Beta adrenergic receptors.

The following table summerises the distribution of receptors in the different organs.

Effector organ	Receptor	Response
Heart		
Sino-atrial node	Beta	Increase in the heart rate.
Atrio-ventricular node	Beta	Increase in conduction velocity and shortening of the functional refractory period.
Atria	Beta	Increase in contractility
Ventricles	Beta	Increase in contractility
Blood vessels		
Skin and mucosa	Alpha	Constriction
Skeletal muscle	Beta	Dilatation
Bronchioles	Beta	Relaxation
Gastro intestinal tract		
i. Motility		
Stomach	Beta	Decrease
Intestine	Beta & Alpha	Decrease
ii. Sphincters		
Stomach	Alpha	Contraction
Intestine	Alpha	Contraction
Urinary bladder		
Detrusor	Beta	Relaxation
Trigone & sphincters	Alpha	Contraction
Eye		
Radial muscle, iris	Alpha	Contraction
Ciliary muscle	Beta	Relaxation

However, 2 exceptions were noted :

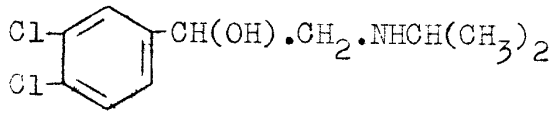
i. The cardiac stimulating effects produced by sympathomimetic amines are mediated entirely by beta receptors.

ii. The inhibitory effects of sympathomimetic amines on the gut are mediated by both alpha and beta receptors.

In contrast to Ahlquist's investigations in which the type of adrenergic receptors was identified by tests of relative potencies of a series of sympathetic amines (that is of sympathetic agonist drugs), the use of sympathetic antagonists offers a more convenient means of defining the nature of adrenergic receptors.

Although, the alpha adrenergic receptor blocking drugs such as ergot derivatives and dibenamine etc..... have been used for many years, agents that are capable of antagonising the beta adrenergic effects of sympathetic amines and of sympathetic nerve stimulation have become available only relatively recently.

Powell and Salter (1958) described the pharmacological properties of dichloroisoproternol "DCI", the first drug that could block the beta adrenergic receptors.

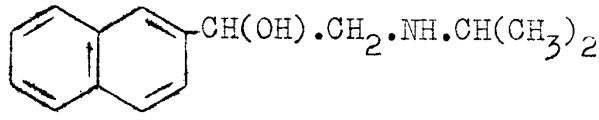


DCI

These investigators found that the concomitant administration of this drug and the alpha blocking agent dibenamine abolished both the vaso constrictor and vaso dilator actions of epinephrine. Thus, they confirmed Ahlquist's hypothesis that the actions of sympathetic amines are mediated by 2 types of receptors and it became clear that each of them could be blocked by a different antagonist.

Though, **DCI** is a potent inhibitor of the beta adrenergic receptors, it is not totaly devoid of intrinsic beta sympathomimetic activity.

Black and Stephenson (1962) discovered that the compound 2-isopropylamino-1-(2-naphthyl) ethanol hydrochloride (Alderlin or Pronethalol), a derivative of isoprenaline, selectively blocks the beta drenergic receptors and has little if any intrinsic alpha or beta sympathomimetic effect.



Pronethalol