Using sympathomimetic drugs to manage hypotension 2: use in clinical practice

An outline of sympathomimetic drugs, the different types and how they are used in certain groups of patients in clinical practice.

**INTRODUCTION**
When caring for certain groups of critically ill patients, it is sometimes necessary to pharmacologically increase and maintain blood pressure. Such patients might include those suffering from shock and hypotension following surgery or those in cardiac failure.

Prolonged cardiac failure-induced hypotension can result in hypoperfusion, cellular and tissue damage, global acidosis and, potentially, multiple organ failure. These harmful effects can increase both morbidity and mortality (Herndon and Wernerman, 2007; Singer, 2007; Singer and Grant, 1999).

In the absence of disease, the parasympathetic and sympathetic divisions of the autonomic nervous system maintain BP and sustain homeostasis. However, in certain disease states, the sympathetic nervous system is unable to sustain normal BP and it becomes necessary to artificially mimic its effects. Drugs used clinically that mimic the effects of the sympathetic nervous system are known as sympathomimetics.

**SYMPATHETIC NERVOUS SYSTEM**
To understand how sympathomimetic drugs work, it is necessary to discuss the sympathetic nervous system and its role in maintaining homeostasis and responses to physiological changes.

The sympathetic (and the parasympathetic) nervous system are parts of the autonomic nervous system (ANS). The word ‘autonomic’ denotes that this part of the nervous system cannot be controlled consciously. Together, the sympathetic and parasympathetic nervous systems regulate individual organ function and maintain homeostasis.

Both the sympathetic and parasympathetic systems consist of myelinated preganglionic fibres, which make synaptic connections with unmyelinated postganglionic fibres. These latter fibres innervate target organs. However, the two systems have anatomical and functional differences.

The sympathetic nervous system is involved in regulating physiological processes such as heart rate, BP, constriction and dilatation of blood vessels and the ‘fight or flight’ response (Neal, 2005). The fight/flight response is also referred to as the sympathico-adrenal response and causes the secretion of adrenaline and, to a lesser extent, noradrenaline. These hormones increase BP, which is needed in certain situations. The parasympathetic nervous system also regulates physiological processes. However, its actions work to decrease heart rate and BP.

Therefore, drugs used to increase BP mimic the sympathetic division of the nervous system, which originates in the spinal cord.

**LEARNING OBJECTIVES**
1. Describe what sympathomimetic drugs are and how they work.
2. Understand the different types and clinical uses of sympathomimetics.

Cell bodies of the first neuron (preganglionic neurons) are located in the thoracic and lumbar regions of the spinal cord, often referred to as the thoracolumbar outflow (Guyton and Hall, 2005). After leaving the spinal cord, preganglionic sympathetic fibres...
pass into one of the ganglia of the sympathetic chain (Guyton and Hall, 2005). The postganglionic neurons then travel to their destinations in the various organs (Fig 1).

**INFORMATION TRANSMISSION**

Sympathetic and parasympathetic nerve fibres all secrete one of the two synaptic transmitters: acetylcholine or noradrenaline (norepinephrine). Those that secrete acetylcholine are said to be cholinergic and those that secrete noradrenaline are said to be adrenergic (Richards et al, 2007; Guyton and Hall, 2005).

All preganglionic neurons are cholinergic. Thus, both sympathetic and parasympathetic preganglionic nerve fibres secrete acetylcholine. Although the postganglionic neurons of the parasympathetic nervous system also secrete acetylcholine and, therefore, remain cholinergic, the postganglionic nerve fibres of the sympathetic nervous system secrete noradrenaline. Thus, sympathetic postganglionic neurons are adrenergic (Fig 2).

For noradrenaline to stimulate a response within an effector organ, it must bind with highly specific receptor sites. According to Guyton and Hall (2005), experimentation with drugs that mimic the action of noradrenaline on sympathetic effector organs have shown there are two types of adrenergic receptors. These are known as alpha and beta receptors, with each being further classified into alpha_1 and alpha_2, and beta_1 and beta_2, (Bear et al, 2006). Table 1 shows the effects of stimulation of the sympathetic nervous system on organs.

Sympathetic adrenergic nerves are found in the heart where they innervate the sino-atrial node and atrio-ventricular node, conduction pathways and myocytes. Thus, some of the effects of sympathetic nerve stimulation include increased heart rate and BP, and vasoconstriction.

**SYMPATHOMIMETICS**

This is a group of drugs whose effect resembles activity in the stimulated sympathetic nervous system, especially of the heart and circulation (Crossman and Neary, 2005). They include drugs that act directly on adrenoreceptors in tissues as well as those that act by releasing noradrenaline from sympathetic nerve terminals.

As such, these drugs work by increasing heart rate and contractility. They include substances such as epinephrine and norepinephrine, as well as synthetic drugs such as phenylephrine.

The properties of the drugs vary depending on the dose used and where each acts.

**Drug action**

Sympathomimetic drugs stimulate the heart by activating beta-adrenergic receptors, and cause vascular smooth muscle contraction and vasoconstriction by activating alpha-adrenergic receptors.

Adrenergic receptors are a group of cell membrane receptors that receive neuronal impulses from postganglionic adrenergic fibres from the sympathetic nervous system (Nestler et al, 2001). These are divided into alpha and beta receptors.

Sympathomimetics are used in conditions where it is necessary to raise BP by stimulating the heart and inducing vasoconstriction (Nestler et al, 2001). They can, therefore, be classified into either inotropic or vasoconstrictor sympathomimetics.

Inotropic sympathomimetics include:
- Dobutamine;
- Dopexamine;
- Isoprenaline;
- Dopamine (rarely used today).

Inotropic sympathomimetics act on receptors in cardiac muscle to increase cardiac contractility. Dobutamine acts on beta_1 receptors and is used to increase the heart’s contractility with little effect on rate. Dopexamine acts on beta_2 receptors and is used to increase contractility, but does not cause vasoconstriction.

Isoprenaline increases both heart rate and contractility but is less selective than the other drugs.

Vasoconstrictor sympathomimetics include:
- Ephedrine;
- Phenylephrine;
- Norepinephrine/noradrenaline.

**TABLE 1. EFFECTS OF SYMPATHETIC OR PARASYMPATHETIC STIMULATION**

<table>
<thead>
<tr>
<th>Sympathetic stimulation</th>
<th>Structure</th>
<th>Parasympathetic stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate increases</td>
<td>(Beta_1 Heart)</td>
<td>Rate decreases</td>
</tr>
<tr>
<td>Myocardial contractility increases</td>
<td>(Beta_2 Heart)</td>
<td>Myocardial contractility decreases</td>
</tr>
<tr>
<td>Bronchial muscle relaxes</td>
<td>(Beta_2 Heart)</td>
<td>Bronchial muscle contracts</td>
</tr>
<tr>
<td>Pupil dilates</td>
<td>Eye</td>
<td>Pupil constricts</td>
</tr>
<tr>
<td>Miotility reduces</td>
<td>Intestine</td>
<td>Digestion increases</td>
</tr>
<tr>
<td>Sphincter closes</td>
<td>Bladder</td>
<td>Sphincter relaxes</td>
</tr>
<tr>
<td>Urine secretion decreases</td>
<td>Kidneys</td>
<td>Urine secretion increases</td>
</tr>
</tbody>
</table>

**FIG 2. POSTGANGLIONIC SYMPATHETIC NEURONS**

ACh or NE: Smooth muscle contraction or relaxation
Cardiac muscle increased or decreased rate and force of contraction
Glands Increased or decreased secretions
ACh or NE: Skeletal muscle contraction

Catherine Hick
Vasoconstrictor sympathomimetics raise BP by acting on alpha-adrenergic receptors to constrict peripheral vessels. These receptors have a powerful vasoconstrictor effect on the skin, mucous membranes, and hepatic and renal system, with little effect on coronary and cerebral circulation (Rang et al, 2003).

Ephedrine has mixed alpha and beta actions that cause vasoconstriction and also increase heart rate (by acting on beta receptors), so it is generally used in certain hypotensive states with associated bradycardia.

Phenylephrine acts by stimulating alpha receptors and is used in acute hypotension and has a long duration of action (its half-life is about 2–3 hours), whereas noradrenaline/norepinephrine has a shorter duration of action (half-life around 5–10 minutes).

Adrenaline stimulates alpha, beta, and beta_2 receptors, resulting in increased heart rate and myocardial contraction. Norepinephrine acts mainly on alpha_1 receptors with few effects on beta receptors, causing a raise in BP, but is less likely to cause tachycardia than adrenaline.

Table 2 summarises the location and action of alpha and beta receptors.

**SYMPATHOMIMETIC USE**

The decision to initiate sympathomimetic therapy is a medical one and will be based on the patient’s clinical needs (see Table 3).

When administering the sympathomimetic drug of choice, nurses need to ensure its therapeutic effect is achieved. Monitoring BP and pulse before administration, frequently during initial dosage, and periodically throughout therapy is important. Reporting significant changes and acting accordingly is vital to a good outcome.

There are a number of issues to consider when initiating sympathomimetic therapy. For example, Rang et al (2003) suggested that their use in hypotension caused by hypovolaemia is controversial. Therefore, the cause of any hypotension should be given careful consideration. For instance, if the condition has resulted from hypovolaemia, then first-line treatment should be fluid replacement.

Sympathomimetic drugs are most useful when hypotension is due to vasodilatation or a result of spinal anaesthesia drugs (Neal, 2005).

Furthermore, sympathomimetic drugs such as dobutamine, isoprenaline and dopexamine increase the myocardium’s contractility. This, in turn, will increase the myocardium’s oxygen demand. Therefore, their use in patients with any degree of cardiogenic shock should be given careful consideration.

These drugs can effectively overcome the prolonged effects of hypotension when used appropriately. Therefore, all nurses working with critically ill patients need to have a good understanding of them.

**REFERENCES**


### TABLE 2. RECEPTOR TYPE, LOCATION AND ACTION

<table>
<thead>
<tr>
<th>Receptor type</th>
<th>Location</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha_1</td>
<td>Vascular smooth muscle</td>
<td>Vasocostruction and increased peripheral resistance</td>
</tr>
<tr>
<td>Alpha_2</td>
<td>Central and peripheral nervous system</td>
<td>Inhibits the release of norepinephrine</td>
</tr>
<tr>
<td>Beta_1</td>
<td>Myocardium</td>
<td>Increased myocardial contractility, tachycardia, and release of renin from the juxtaglomerular apparatus of the kidney</td>
</tr>
<tr>
<td>Beta_2</td>
<td>Bronchial and vascular smooth muscle</td>
<td>Vasodilatation of bronchioles and peripheral vessels and causes decreased peripheral resistance</td>
</tr>
</tbody>
</table>

### TABLE 3. COMMON SYMPATHOMIMETIC DRUGS AND THEIR USES

<table>
<thead>
<tr>
<th>Sympathomimetic drug</th>
<th>Clinical use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dobutamine</td>
<td>This is administered to increase cardiac output in patients with congestive heart failure as it increases myocardial contractility. Also given in other conditions to increase cardiac output</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Low dosage is used to increase renal blood flow. High dosage is used to increase BP as in hypotension or shock states</td>
</tr>
<tr>
<td>Dopaexamine</td>
<td>Inotropic and chronotropic effect, used in heart failure</td>
</tr>
<tr>
<td>Isoprenaline</td>
<td>Increases both heart rate and contractility, used in complete heart block, also severe bradycardia which is unresponsive to atropine</td>
</tr>
<tr>
<td>Ephedrine</td>
<td>Hypotension following spinal/epidural anaesthesia, transient hypotension</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>Acute hypotension</td>
</tr>
<tr>
<td>Norepinephrine/noradrenaline</td>
<td>Hypotension and septic shock-induced vasodilatation</td>
</tr>
<tr>
<td>Epinephrine/adrenaline</td>
<td>Acute hypotension, cardiac arrest</td>
</tr>
</tbody>
</table>