Dysautonomia and It's Perioperative Implications

Essay

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Mostafa Mohammed Salaheldeen Faheem

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List of Abbreviations

AGEs	:	Advanced glycation end products
AH	:	Autonomic Hyperreflexia
AIDP	:	Acute inflammatory demyelinating polyneuropathy
ANS	:	Autonomic Nervous system
CNS	:	Central nervous system
FAP	:	Familial amyloid polyneuropathy
GBS	:	Guillain-Barré syndrome
HR	:	Heart rate
HRV	:	Heart Rate Variability
LEMS	:	Lambert-Eaton myasthenic syndrome
MSA	:	Multiple System Atrophy
POTS	:	Postural Orthostatic Tachycardia Syndrome
SPT	:	Serine Palmitoyltransferase

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Introduction

Severe autonomic failure occurs in about 1 in 1000 people. Such patients are remarkable for the striking and sometimes paradoxical responses that manifest to a variety of physiologic and pharmacologic stimuli. Autonomic failure may be secondary to other diseases, such as diabetes mellitus, amyloidosis, or bronchogenic carcinoma; or be due to a primary autonomic disorder such as multiple system atrophy (MSA; Shy-Drager syndrome) or pure autonomic failure ***(Goldstein et al., 2002; Shibao et al., 2007)***.

Proper functioning of the autonomic nervous system requires that both afferent and efferent limbs are intact. Afferent neurons detect changes in blood pressure, temperature, and the myriad of other vital processes controlled by the autonomic nervous system, and communicate these changes centrally; whereas the efferent neurons engage effector systems to perturb or restore homeostasis. Dysfunction of the afferent limb is typically associated with labile hypertension, as seen in baroreflex failure, particularly in the postoperative period after endarterectomy or other neck surgeries affecting the carotid sinus nerve ***(Robertson et al., 1993)***.

Abnormalities of central autonomic pathways such as in patients with MSA, of efferent effector systems as in patients with pure autonomic failure, patients with deficiency of dopamine beta hydroxylase, or any combination thereof can all lead to clinical autonomic failure and disabling orthostatic hypotension ***(Mustafa et al., 2012)***

Some of the most severely affected individuals have pure autonomic failure or multiple system atrophy. Such patients often have both extremely low blood pressures

upright and extremely high blood pressures supine. Patients with MSA are perhaps the most vulnerable of all such patients to the complex and interacting responses to drugs and perturbations that occur during anesthesia ***(Robertson, 2008)***.

Aim of the work

The aim of this essay is to review the pathophysiology and clinical features of dysautonomia and how to evaluate patients suffering from it and perioperative anesthetic considerations for patients with dysautonomia.

Chapter I
Autonomic Nervous System

Many anaesthetic procedures and drugs used in anaesthetic practice have a direct influence on the autonomic nervous system. It is therefore essential that the anaesthetist should have a basic understanding of its structure and function ***(Pratt & Gwinnutt, 2005).***

Many bodily functions proceed without any conscious supervision from our central nervous system (CNS). For example, we don't have to remember to digest our food after a meal, or sweat when too warm. These functions are controlled subconsciously, with a degree of automaticity, by a branch of the nervous system; the *Autonomic Nervous system* (ANS) ***(Pratt & Gwinnutt, 2005).***

The ANS can thus be thought of as the regulatory system that partly or wholly controls most of the body's organ systems and homeostatic mechanisms. In general, ANS effects are involuntary, relatively rapid, neuronal reflexes ***(Guyenet, 2006).***

The afferent input to the reflex arc varies and can be from:

i) The Autonomic Nervous System; for example the tachycardia in response to hypotension is mediated by baroreceptors.

ii) The Central Nervous System; for example the "vaso-vagal response" to impending cannulation in a needle-phobic patient.

The efferent limb of neuronal autonomic reflexes consists of specific primary autonomic nerves that synapse in

autonomic ganglia, with secondary or "postganglionic" fibers. These postganglionic fibers mediate the desired response at the effector organ ***(Hall, 2011).***

The "effector limb" of the ANS is subdivided in to 2 separate divisions; the sympathetic, and parasympathetic nervous systems. These two divisions differ in both structure and function ***(Hall, 2011).***

In general the sympathetic nervous system can be thought of as preparing the body for "fight or flight". In the cardiovascular system, it causes increased inotropic and chronotropic drive that lead to increased cardiac output and blood flow is routed toward vital organs and skeletal muscle. In addition, it leads to an overall increase in CNS stimulation, and respiratory drive. Meanwhile, it cause decrease in visceral activity ***(McCorry, 2007).***

The parasympathetic nervous system in contrast, increases the activity of the abdominal viscera. The cardiovascular system is depressed; reducing heart rate and cardiac output, and routing blood flow toward visceral beds. The respiratory system and CNS are depressed ***(McCorry, 2007).***

Structure of the Autonomic Nervous System

In addition to its close functional relationship to the central nervous system, the ANS shares a close anatomical proximity. In the sympathetic nervous system, the ganglia are fused to form the sympathetic chain, which lies adjacent to the spinal column throughout most of its length. Pre-ganglionic sympathetic fibers have cell bodies in the intermedio-lateral horn of grey matter in the spinal cord between T1 & L2. These fibers emerge from the spinal cord in the primary ventral rami of the spinal nerves and pass to

the sympathetic chain via the *white rami communicants.* In the sympathetic chain the fibers will synapse, giving rise to unmyelinated post-ganglionic fibers that rejoin the spinal nerves via the *grey rami communicants*. Some pre-ganglionic fibers however ascend or descend to other levels of the sympathetic chain prior to synapsing. In general therefore, sympathetic pre-ganglionic fibers are short, and postganglionic fibers tend to be longer ***(Furness, 2006).***

Parasympathetic pre-ganglionic fibers leave the CNS in both cranial and sacral nerves; the so-called "cranio-sacral outflow". Cranial fibers arise from specific parasympathetic brainstem nuclei of cranial nerves III, VII, IX, and X. The fibers travel with the main body of the cranial nerves to ganglia that tend to be more distant from the CNS and close to the target organ. Consequently, in contrast to the sympathetic nervous system, pre-ganglionic fibers tend to be long, whereas post-ganglionic fibers will be shorter ***(Pratt & Gwinnutt, 2005).***

Sacral pre-ganglionic fibers emerge from the CNS via the ventral rami of nerves S2-S4 and form the pelvic splanchnic nerves, which pass to ganglia close to the effector organs ***(Gibbins, 2004).***

The basic structure of the ANS is illustrated in the diagram below:

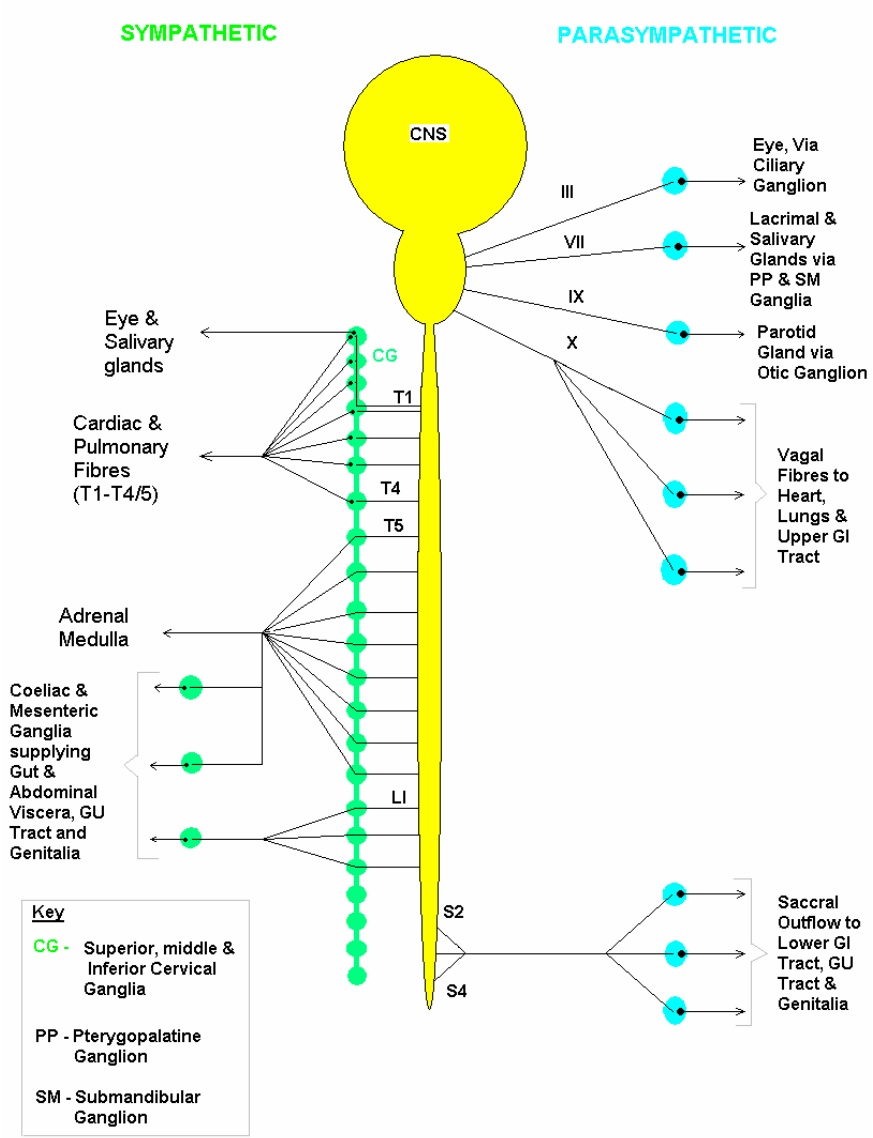

Fig. (1): Basic Structure of the Autonomic Nervous System ***(Pratt & Gwinnutt, 2005)***

One can imagine, that given the anatomical differences between the 2 divisions, anaesthetic interventions may have a greater or lesser effect on the sympathetic or parasympathetic nerves. A good example of this can be seen during spinal anaesthesia ***(Pratt & Gwinnutt, 2005).***

A spinal block will temporarily halt input to the sympathetic afferents at the affected levels, leading to vasodilatation and loss of sweating in the affected dermatomes. If the block is allowed to spread to the levels supplying cardiac sympathetic fibers (T1-T4/5), there will be a loss of both inotropic and chronotropic drive to the heart and progressive hypotension. The parasympathetic supply to the heart coming from the vagus nerve will be unaffected by the spinal block, leading to unopposed parasympathetic stimulation and a bradycardia ***(Alexander et al., 2004).***

Physiology of the Autonomic Nervous System

In order to understand the functions of the ANS, and the possible targets for pharmacological manipulation, it is necessary to have a basic knowledge of the neurotransmitters and receptors, which are integral to the ANS. As with all neuronal systems, the effects of the ANS are mediated by the release of neurotransmitters. Pre-ganglionic fibers of both the sympathetic and parasympathetic nervous systems secrete acetylcholine, thus nicotinic receptors predominate in the autonomic ganglia. Sympathetic postganglionic fibers are mostly adrenergic in nature, i.e. secreting noradrenaline and occasionally adrenaline. The effect of post-ganglionic nerve stimulation will depend upon the receptors present at the effector site, usually alpha and beta adrenoreceptors. The effects are terminated by noradrenaline re-uptake in to the nerve terminals ***(Jänig, 2006).***

A special case within the sympathetic nervous system is the nerve to the adrenal medulla. This nerve does not synapse within the sympathetic chain and hence is strictly still "pre-ganglionic" when it reaches the adrenal medulla and consequently secretes acetycholine. The adrenal medulla, which can be thought of as a modified autonomic ganglion, in turn secretes adrenaline in to the systemic circulation ***(Alexander et al., 2004).***

Parasympathetic post-ganglionic fibers release acetylcholine. Most effects are mediated via muscarinic receptors and actions are terminated by hydrolysis of acetylcholine by acetylcholinesterase within the synaptic cleft ***(Jänig, 2006).***

Neurotransmitters bind with specific receptors at target cells to produce their effects *(Fig. 2)*. Different receptor subtypes exist in each of the divisions of the ANS, and the intracellular response in the target cell and hence the target organ is specific to the receptor type. Within the sympathetic nervous system, effects are generally mediated by adrenoreceptors. In the parasympathetic system effects are mediated generally by muscarinic acetylcholine receptors. A further special case is that of sympathetic post-ganglionic fibers supplying sweat glands. These fibers secrete acetylcholine and exert their effects through muscarinic receptors ***(Pratt & Gwinnutt, 2005).***