Influence of Inhalation Anaesthetics on the Autonomic Nervous System

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Introduction

Inhalation anaesthesia and various stressful events associated with surgery may severely alter the function of the autonomic nervous system. Almost all investigations of the influence of inhalation anaesthetics on autonomic nervous activity deal with the effects of these drugs on the sympatho-adrenal system, and on the baroreceptors which are the sensory organs for the afferent limb of baroreceptor reflexes. This predominant interest in the sympathetic division of the autonomic nervous system is due to the attempts to relate the main side-effects of these drugs on the cardiovascular system to changes in autonomic nervous activity. Thus hypo- or hypertensive reactions may occur during inhalation anaesthesia; in this connection it is of interest that changes in blood-pressure due to alterations of arteriolar resistance can be related to an increase or decrease in sympatho-adrenal activity; by contrast, cholinergic impulses are virtually devoid of physiological significance in this respect. Furthermore, inhalation anaesthetics are known to cause a negative inotropic effect; again, the force of contraction of the cardiac ventricles is effectively controlled by the sympathetic but not by the parasympathetic nervous system. The present report will therefore concentrate on the effects of inhalation anaesthetics on the sympatho-adrenal system and on the baroreceptor reflexes. However, it should be pointed out that a reduction of the sympathetic tone causes a predominance of parasympathetic nervous activity. In this situation the administration of atropine is absolutely necessary to avoid serious dysfunction of various organ systems.

Controversial results concerning the influence of inhalation anaesthesia on plasma adrenaline (A) and noradrenaline (NA) have been reported, although the specificity and sensitivity of the methods used for determination of plasma catecholamines (CA) were considerably improved by introduction of radioenzymatic techniques. For instance, Roizen et al. [31] found a decrease in plasma NA in rats anaesthetized with halothane, whereas Da Prada et al. [8] observed an increase; Stokke et al. [37] reported no change and Balogh et al. [3] a slight increase in plasma CA during halothane-nitrous oxide anaesthesia in man. In all of these investigations radioenzymatic methods were used for determination of plasma CA.

In the present report the possible reasons for these and similar discrepancies found with other inhalation anaesthetics will be discussed. For this purpose some of the pharmacodynamic effects of these compounds on the baroreceptors and on discrete functional levels of the sympatho-adrenal system will be reviewed. It is not the intention to consider each compound as a pharmacological entity, but to analyse the principles and common features of their actions. Mainly data obtained with halothane, enflurane, and methoxyflurane will be reported, and a major part of this presentation will be devoted to personal experimental in-
vestigations in this field. Moreover, additional influences on the sympatho-adrenal system which occur during inhalation anaesthesia but which are not caused by these compounds themselves will be considered. Finally, by integration of all synergistic and antagonistic influences, conclusions will be drawn concerning the overall effects of inhalation anaesthetics on sympatho-adrenal activity, which are reflected by changes in plasma catecholamines.

Effects on Baroreceptors

A decrease in blood-pressure causes decreased stimulation of baroreceptors in the aorta and carotid sinus, resulting in a decreased impulse flow via afferent nerve fibres to the vasomotor centres in the brain-stem, and finally in an increased sympatho-adrenal output to the effector sites. Halothane and enflurane have been shown to cause a sensitization of the baroreceptors [4, 22]. Thus, at a given level of blood-pressure, the anaesthetics increase discharge via afferent fibres, and a higher level of blood-pressure than the real one is signalled to the central nervous system. On the other hand, since the main site of action of halogenated inhalation anaesthetics underlying the decrease in blood-pressure appears to be the cardiovascular system itself, an inhibition of impulse flow from the baroreceptors resulting in reflex activation of the sympatho-adrenal system only occurs if the hypotensive effect overcomes the sensitization of the baroreceptors.

Effects on the Central Nervous System

In cats halothane decreased the preganglionic sympathetic activity, but the anaesthetic had little effect on the response of preganglionic sympathetic neurones to baroreceptor stimulation [36]. These results indicate that the anaesthetic causes a depression of the central sympathetic tone, but that this effect is rather weak. Moreover, the authors postulate that the compound acts predominantly on the pressor elements of the medullary vasomotor centre. The results obtained with enflurane were very similar to those reported for halothane [24, 35], whereas the effects of methoxyflurane were less pronounced; with this anaesthetic a slight reduction in preganglionic sympathetic activity could only be observed in baroreceptor-denervated cats [34]. Interestingly, in cats anaesthetized with enflurane or methoxyflurane, addition of nitrous oxide caused an increase in pre-ganglionic sympathetic discharge [24].

Effects on Sympathetic Ganglia and the Adrenal Medulla

There is no doubt that halothane is capable of blocking transmission in sympathetic ganglia. This has already been established by early work of Biscoe and Millar [5] in cats and rabbits, and of Price and Price [29] in dogs (in this connection see also the reviews by Alper and Flacke [1] and Gardier [10]). Interestingly, halothane markedly inhibited the response to dimethylphenylpiperazinium (DMPP), a nicotinic receptor agonist, leaving unchanged the response to McN-A-343, a muscarinic receptor agonist; these findings indicate that halothane specifically inhibits the responses mediated by post-synaptic nicotinic ganglionic receptors [2]. Although there exist only few reports on the effect of methoxyflurane on sympathetic