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BRIEF COMMUNICATION

Comparison of α-MSH and Several Vasoactive Substances on Vascular Resistance in the Feline Mesenteric Vascular Bed[1]

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KADOWITZ, P. J., B. M. CHAPNICK AND A. J. KASTIN. *Comparison of α-MSH and several vasoactive substances on vascular resistance in the feline mesenteric vascular bed.* PHARMAC. BIOCHEM. BEHAV. 5(2) 219–221, 1976. – The effects of α-MSH and several other vasoactive substances on the mesenteric vascular bed were studied in the anesthetized cat under conditions of controlled blood flow. Intra-arterial injections of α-MSH in doses of 10, 30, and 100 μg resulted in significant dose-related decreases in mesenteric arterial perfusion pressure but little or no effect on systemic arterial pressure. The vasodilator response to α-MSH was brief in duration and resistance to flow was decreased 10, 18, and 26 percent at 10, 30, and 100 μg. These significant changes after α-MSH were of a much smaller magnitude than were observed after prostaglandins E_1 and E_2, isoproterenol, bradykinin or glyceryl trinitrate and differed completely from the increased resistance after angiotensin II and norepinephrine.

Mesenteric vascular bed α-MSH Peptides Prostaglandins

THE pituitary hormones adrenocorticotropin (ACTH) and melanocyte stimulating hormone (MSH) are closely related chemically. The amino acid sequence of the tridecapeptide α-MSH is identical to the N-terminal sequence 1–13 of ACTH. Both MSH and ACTH had a positive chronotropic effect in the dog heart-lung preparation and this action was not dependent on the sympathetic nervous system since treatment with reserpine did not abolish the effect [6]. In the anesthetized dog, MSH increased heart rate and myocardial contractile force, even after treatment with the β-adrenergic receptor blocker propanolol [1]. In addition to its positive inotropic and chronotropic effects, α-MSH had antiarrhythmic activity in the dog [7]. Furthermore, α-MSH and several synthetic corticotropin polypeptides decreased blood pressure in the cock [3] and α-MSH decreased regional blood flow to most areas of the brain in the rat except the occipital cortex [2]. However, the effects of α-MSH on vascular resistance have not been quantified. The purpose of the present investigation was to study the effects of α-MSH on a peripheral vascular bed, namely the mesenteric circulation, in the anesthetized cat under conditions of controlled blood flow. In addition, the effects of α-MSH in the mesenteric vascular bed were compared to those of several vasoactive peptide hormones and other substances.

METHOD

Adult cats of either sex weighing 1.9–3.4 kg were anesthetized with pentobarbital sodium 30 mg/kg intraperitoneally and the trachea was intubated to ensure a patent airway. Systemic arterial pressure was measured from a catheter in the carotid artery and intravenous injections of heparin and supplementary doses of the anesthetic were made into a catheter in the jugular vein. Constant flow perfusion of the mesenteric artery was established by inserting catheters into the abdominal aorta and the superior mesenteric artery. Blood was withdrawn from the abdominal aorta and pumped into the mesenteric arterial catheter at controlled flow by a Sigmamotor pump. Mesenteric arterial perfusion pressure was measured from a lateral tap on the perfusion tubing between the pump and the mesenteric catheter. The pumping rate averaged 41 ml/min and was not changed during the experiment. All pressures were measured with Statham P23AC transducers and recorded on a Grass model VII polygraph. Norepinephrine hydrochloride (Sigma), isoproterenol hydrochloride (Sigma), bradykinin triacetate (Sigma), angiotensin II (Ciba), prostaglandin E_1 (PGE_1) and PGE_2 (Upjohn), glyceryl trinitrate (Lilly), and synthetic α-MSH (10^7 U/mg) were injected into the perfusion circuit near the mesenteric

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artery. The hemodynamic data were evaluated using methods of Snedecor [8] for paired comparison. A p value of less than 0.05 was considered significant.

RESULTS

The effects of α-MSH on the mesenteric vascular bed are illustrated in Fig. 1. Intra-arterial injection of α-MSH as a bolus directly into the perfusion circuit in doses of 10, 30 and 100 μg resulted in a dose-related decrease in mesenteric arterial perfusion pressure ($p<0.05$ at each dose). This was not associated with any meaningful change in systemic arterial pressure which was 118 ± 12 mm Hg in the control period and was 116 ± 15 mm Hg after injection of the 100 μg dose ($p>0.1$). Since blood flow in the mesenteric circulation was maintained constant by a pump, the decrease in mesenteric arterial perfusion pressure reflected a decrease in vascular resistance in the mesenteric circulation. The vasodilator response was rapid in onset but brief in duration, in that perfusion pressure returned to the control value in 10–30 sec.

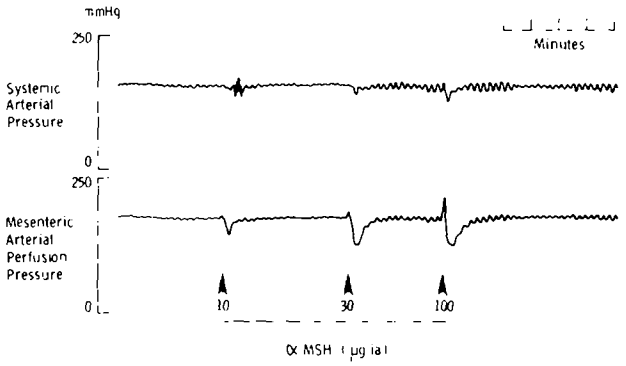

FIG. 1. Tracings from an experiment illustrating the effects of α-MSH on feline mesenteric arterial perfusion pressure and systemic arterial pressure. α-MSH was injected directly into the arterial perfusion circuit as a bolus in doses of 10, 30, and 100 μg.

The vasodilator responses to PGE_1, PGE_2, bradykinin, isoproterenol, glyceryl trinitrate, and α-MSH in 6–8 cats are compared in Fig. 2. All of these substances were far more active vasodilators than α-MSH. PGE_1 was the most potent vasodilator in the group, whereas PGE_2, bradykinin and isoproterenol were slightly less active than PGE_1. All of these compounds were more potent than glyceryl trinitrate which exerted a greater effect than α-MSH.

The effects of angiotensin II and norepinephrine on the mesenteric vascular bed also were examined. Table 1 indicates that in a series of 4–5 cats, angiotensin II and norepinephrine and marked vasoconstrictor activity in the mesenteric vascular bed, not vasodilator activity.

DISCUSSION

The results of this study show that α-MSH possesses significant vasodilator activity in the feline mesenteric vascular bed. The effects of α-MSH on the mesenteric vascular bed were dose-related and were brief in duration. In terms of relative potency, considerably greater vasodilator activity was observed after administration of prostaglandins E_1 and E_2 (lipids), bradykinin (a nonapeptide), isoproteranol (a β-adrenergic stimulant), and glyceryl trinitrate (a nonspecific vasodilator agent) than after α-MSH. In contrast to these agents which were vasodilators, angiotensin II (an octapeptide) and norepinephrine (an alpha adrenergic stimulant) were potent vasoconstrictors in the mesenteric vascular bed.

Although α-MSH had a relatively weak vasodilator action on mesenteric vessels, the doses per kg of body weight injected locally into the mesenteric circulation of the cat were similar to the doses which resulted in behavioral and EEG changes after intraperitoneal injection in rats [5]. It is difficult to compare doses administered by different routes in different species, but if systemic vascular changes occur in association with CNS changes, the possibility of a causal relationship might be considered. Regardless, this study demonstrates that the extra-endocrine effects of MSH, like those of the hypothalamic peptides [4], are not confined to the brain.

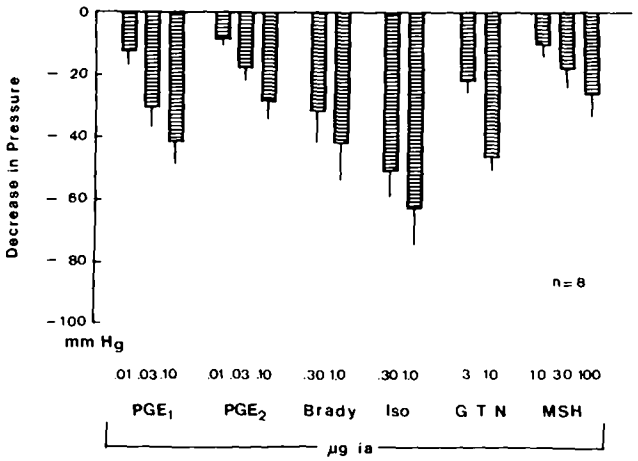

FIG. 2. Bar graph comparing vasodilator responses to PGE_1, PGE_2, bradykinin (Brady), isoproterenol (Iso), glyceryl trinitrate (GTN), and α-MSH in the mesenteric vascular bed of 8 cats. Although all doses of each vasoactive substance were not given in each animal, every agent was injected in at least 6 animals. All changes in perfusion pressure shown in this graph were significantly ($p<0.05$) different from control values.

TABLE 1

EFFECT OF ANGIOTENSIN II AND NOREPINEPHRINE ON THE MESENTERIC VASCULAR BED

Dose (μg)	Mean (± SE) Increase in Mesenteric Arterial Perfusion Pressure (mm Hg)
Norepinephrine (n=5)	
0.3	44 ± 4*
1.0	72 ± 6*
3.0	102 ± 4*
Angiotensin (n=4)	
0.3	69 ± 10*
1.0	100 ± 17

*Significantly different from control values ($p<0.05$).

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