Intracerebroventricular administration of Hemin elicits febrile response

Park HJ°, Lee SH, Park HY, Lee SY

Lab. of Pharmacology, College of Pharmacy, Sungkyunkwan University, Suwon

It is widely accepted that inflammation and exogenous pyrogens evoke fever through the activation of macrophages to release endogenous pyrogenic cytokines (IL-1β, IL-6 and TNF-α) and the ending step in febrile response is the action of a PGE2 on thermoregulatory pathways in the hypothalamus. However, the precise mechanism by which blood-borne cytokines increase PGE2 synthesis in hypothalamus is still unclear. Recently, nitric oxide (NO) was proposed as a possible signal transducer of circulating pyrogen-induced PGE2 synthesis in hypothalamus. In our previous study, i.c.v. administration of exogenous carbon monoxide (CO), which has very similar character with NO in biological activity, markedly increased the body temperature. So, we study the effects of hemin, which is a substrate of CO-producing enzyme (heme oxygenase, HO) and a inducer of HO, on body temperature in this study. Hemin(i.c.v.) markedly increased in body temperature and this response was blocked by ZnPP IX (inhibitor of HO), indomethacin, or cycloheximide (inhibitor of gene transcription). Hemin maximally induced HO-1 in hypothalamus at 3 hrs after administration.
These results suggest that hemin-induced pyresis is partially due to induction of HO-1 and endogenous CO is a possible signal transducer of febrile response in hypothalamus.

[PA1-38] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Effects of long-term administration of NOS inhibitor on aortic contractility

Park HY°, Lee SY

Lab. of Pharmacology, College of Pharmacy, Sungkyunkwan University

Nitric oxide (NO) is one of the important modulators that control vascular smooth muscle tone. The chronic inhibition of NO synthase (NOS) elicits the hypertension in rats. However, the mechanism of hypertension induced by chronic inhibition of NOS is not clear. Thus, to clarify the mechanisms of occurance of hypertension, we studied the effects of adrenergic agents on aortic contractility in rats treated with NOS inhibitors for 21 days were examined.
Chronic administration of L-NAME significantly increased in the blood pressure. The pressor effect of norepinephrine and the depressor effect of prazosin were significantly increased in the L-NAME-induced hypertensive rats. Phenylephrine, a α-receptor agonist, AlF_4^-, G-protein stimulator, elicited the more potent contraction in the aorta of the rats treated with L-NAME for 21 days than in the aorta of the untreated rats. The potentiation of contractile action of phenylephrine by treatment with L-NAME for 21 days was significantly reduced in the endothelium-free aorta. However, the contractile action of phenylephrine was still more potent in the endothelium-free aorta of the rats treated with L-NAME for 21 days than in the endothelium-free aorta of the untreated rats. These results suggests that the hypertension by choronic inhibition of NOS is partially due to the changes of the intracellular signal transduction system of aortic smooth muscle.

[PA1-39] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Interrelationship between the IL-1β-induced pyresis and heme oxygenase in hypothalamus

Park HJ°, Lee SY