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Peripherally acting mediators of pain and analgesia potentiate the central analgesic effects of Fentanyl and Dipyrone in rats

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In recent years, for the treatment of inflammatory and neuropathic pain have been proposed peripherally acting analgesics, being endogenous mediators analgesia (morphine-6-glucuronide, loperamide, adenosine) It is generally accepted that peripheral acting analgetics eliminate pain in result of stimulation of peripheral receptors in the site of inflammation. We have earlier demonstrated that preliminary anesthesia of gastric mucosa by lidocaine and also subdiaphragmatic gastric vagotomy prevents the development of analgesia induced by intramuscular injection of epinephrine, phenylephrine, adenosine cholecystokinin and ATP in the tail-flick test in rats. As shown in the study, Intramuscular administration the Minimum Effective Dose (MED) of central analgesics fentanyl and dipyrone, and the mediators of pain Cholecystokinin (CCK), glutamate, ATP, phenylephrine and mediator analgesia adenosine weakly penetrating into the CNS, induces the maximum analgesic effect in the tail-flick test in rats. MED of dipyrone and fentanyl was reduced in 50-220 times in the case of combined intramuscular injection of each of the analgesics with CCK, glutamate, ATP, adenosine and adrenaline in the threshold, independently non-effective doses (1/10 MED). Intragastric administration of lidocaine and the subdiaphragmatic gastric vagotomy completely eliminate the analgesic effect of the above combinations. The results of these experiments led to the conclusion that peripherally acting mediator agents: adenosine, ATP, phenylephrine, CCK and glutamate when administered systemically cause potentiation of the central analgesic effectof fentanyl and dipyrone as a result of stimulation of the chemoreceptors of vagal afferents in gastric mucosa in a very low threshold doses that it has no significant effect on peripheral nociceptors.

Biography

V E Gmiro is the leading Researcher of Institute Experimental Medicine, Russia. He has published more than 100 papers in reputed journals. His main scientific interest concerns the chemistry and pharmacology of biologically active compounds. He is the USSR State Prize Winner for the investigations in the field of physiology of synaptic transmission. He has been working on the problem of the creation of adaptogenic drugs acting through activation of afferent nerves.

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