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The present study was attemted to invesigate the characteristics of epibatidine on secretion of catecholamine (CA) in the isolated perfused rat adrenal gland and to establish the mechanisim of action. Epibatidine (3 ηM) injected into an adrenal vein produced a great response of in CA secretion from the perfused rat adrenal gland. However, upon the repeated injection of epibatidine (3 ηM) at 15 min intervals, Ca secretion was rapidly decreased after 2nd injection of epibatidine. However, there was no difference between CA secretory responses of both 1st and 2nd periods by the successive administration of epibatidine at 120 min-intervals. Tachyphylaxis to releasing effects of CA evoked by epibatidine was observed by the repeated administration. Therefore, in all subsequent experiments, epibatidine was not administered successively more than 120 min-intervals. The epibatidine-induced CA secretion was markedly inhibited by the pretreatment with atropine,chlorisondamine, pirenzepine, nicardipine, TMB-8, and perfusion of Ca2+-free krebs solution containing EGTA, while was not affected by diphenhydramine. Moreover, the CA secretion evoked by ACh for 1st period(0-4min)was potentiated by the simultaneous perfusion of epibatidine (1.5 ηM), but followed by great reduction immediately after 2nd period. The CA release evoked by high potassium(5.6 ηM) for 1st period (0-4 min) was also enhanced by the simultaneous perfusion of epibatidine, but those immediately after 2nd period were not affects. Taken together, these experimental data suggest that epibatidine causes catecholamine secretion in a calcium dependent fashion from the perfused rat adrenal gland through activation of neuronal cholinergic (nicotine and muscarinic) receptors location in adrenomedullary chromaffin cells. It also seems that epibatidine-evoked catecholamine release is not relevant to activation of cholinergic histaminergic receptors.

[PA1-6] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Evaluation of COX-2 expression in human gastric tumors and COX-2 suppression by aspirin and SC-236 in human gastric cancer cells in vitro.

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Over-expression of cyclooxygenase (COX)-2 has been observed in various tumors and specific COX-2 inhibitors are being tested in clinical trials for colon cancer prevention. In this study, COX-2 expression in gastric tumors and the effect of non-specific (aspirin) and specific (SC-236) COX-2 inhibitors in human gastric cancer cell lines in vitro were studied. COX-2 protein was expressed in ~80% and ~20% of glandular epithelial (GE) cells in tumor tissue (T) and adenomatous polyp, respectively, and mainly localized in the luminal side. No expression was seen in atrophic gastritis. Infiltrated inflammatory cells showed over-expression of COX-2 protein. COX-1 protein expression was negligible in all tissues. COX-2 mRNA level by RT-PCR was higher in T than the adjacent normal tissue. The basal levels of COX-2 mRNA and protein showed different rank orders among four human gastric cancer cell lines, among which SNU-216 showed significant level of both mRNA and protein and was selected for in vitro exp. The suppression of COX-2 mRNA was shown after 24 hr and 48hr at 10 mM and 5mM of aspirin, respectively. Compared to COX-2, COX-1 protein was expressed at a lower level and suppressed by lower conc of aspirin (1mM vs 20 mM) after 48hr exposure. PGE2 production decreased to 50% after 24hr exposure at 20mM of aspirin as determined by EIA. COX-2 protein expression was suppressed after exposure to 1 mM of SC-236 for 48hr. The cytotoxic $IC_{50,72hr}$ was 14.9 mM as measured by XTT and at this conc, apoptosis was induced after 12hr shown by DAPI staining. In summary, over-expression of COX-2 mRNA and protein was observed in pt tumors and cancer cell lines, and SC-236 showed potent cytotoxicity via apoptosis and effectively suppressed COX-2 protein expression. These data indicate that (1) COX-2 over-expression may contribute to carcinogenesis of gastric cancer and (2) studies on the detailed molecular mechanisms of this selective COX-2 inhibitor are needed.