Contractile response of canine gallbladder and sphincter of Oddi to substance P and related peptidesin vitro

Guo, Yan –Shi; Singh, Pomila; Gomez, Guillermo; Rajaraman, Srinivasan; Thompson, James C.

Abstract

Substance P (SP) is a neurotransmitter peptide that is widely distributed in the body. Since SP has been demonstra in the gallbladder (GB) and bile ducts of dogs, it may have a role in biliary motility. The objective of this study was to examine the effect of SP on the GB and sphincter of Oddi (SOD) of dogs in vitro,to evaluate the structure-activity relationship of SP, and to compare the contractile effect of SP with that of cholecystokinin octapeptide (CCK-8) and acetylcholine (Ach). Isolated longitudinal strips of GB and SOD from dogs were suspended in oxygenated Krebs buffer and the isometric tension responses to various doses of CCK-8, Ach, SP, and SP homologs [SP-free acid (SPFA), Octa-SP (O-SP), physalaemin (PHY)] were measured. We found that all the SP homologs, other than SPFA, stimulated GB and SOD contractions in vitroin a dose-dependent manner. The potency of SP and its homologs on GB and SOD was SP ≥PHY > O-SP; SPFA was without effect. CCK-8 was significantly more effective than SP on GB contraction, but unlike SP, CCK had no effect on SOD. The maximum contraction achieved by Ach was 1.3 (SOD) to 2.3 (GB) times greater than that achieved by SP, but the ED 50 of SP was approximately 100- to 200-fold lower than that of Ach. The contractile effect of SP was partially blocked by 10 −5 M atropine. We suggest from the above results that contractile effects of SP on the dog GB and SOD are probably mediated through binding to specific SP receptors that require the C-terminal amino group and the C-terminal penta-peptide sequence in order to be most effective.

Keywords gallbladder, sphincter of Oddi, substance P, acetylcholine, cholecystokinin, motility