HERPES SIMPLEX VIRUS-1 INFECTION ALTERS THE CARBACHOL- AND KCL-INDUCED CONTRACTIONS IN RAT SMALL INTESTINE

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Background Infection by pathogens is considered to play a role in irritable bowel syndrome (IBS), a widespread gastrointestinal (GI) disorder. Among common pathogens herpes simplex virus-1 (HSV-1), orally inoculated to laboratory animals, targets neurons in the enteric nervous system (ENS) and is involved in the pathogenesis of GI disorders. The aims of the present study were to establish an *in vivo* model of HSV-1 infection in the rat intestine and to evaluate possible effects of this virus on intestinal motility. **Methods** Chronic HSV-1 infection was established by inoculating rats intranasally (10^3 pfu) and again intragastrically (i.g., 10^8 pfu) 4 weeks (wk) later. Infected or mock infected rats were sacrificed 1, 2, 4 and 6 wk after the i.g. inoculation. The presence of HSV-1 infection was determined by PCR amplification of HSV-1-tk gene, RT-PCR for HSV-1 latency associated transcripts (LATs) and early gene ICP-4, *in situ* hybridization and immunofluorescence for glycoprotein-C (gC). In isolated ileum and duodenum segments (2 cm), mounted vertically in organ baths, changes in muscle tension were recorded using isometric transducers. Concentration-response curves to carbachol (0.01-100 µmol/L) and to KCl (3-80 mmol/L) in the presence or absence of indomethacin (1 µM) were obtained cumulatively. **Results** Both controls and HSV-1 infected rats did not show clinical and histological abnormalities in the GI tract. In the brain, full-thickness gut and isolated neurons a latent HSV1 infection was shown by the presence of viral tk-DNA and LAT mRNA and by the absence of ICP-4 mRNA transcripts and HSV-1gC immunoreactivity, whereas *in situ* hybridization showed HSV-1 DNA in central nervous system and ENS. In respect to controls, the E_{max} values of carbachol-induced contractions significantly increased by 70% and 97% in the ileum at 1 wk and 6 wk postinfection (PI) and by 92% and 54% in the duodenum at 1 wk and 2 wk PI. Pretreatment with indomethacin decreased by 41 % the E_{max} values determined in the ileum 1 wk and 6 wk PI. Maximum response to KCl was reduced by 61% at 1 wk in the ileum and by 44% and 37% at 1 wk and 4 wk, respectively, in duodenum preparations. The effect of KCl was not influenced by indomethacin. **Conclusions** Following i.g. delivery, HSV-1 establishes a latent infection in the ENS and also significantly impairs intestinal smooth muscle responsiveness to membrane depolarization by KCl while increasing its sensitivity to muscarinic receptor stimulation. Induction of cyclooxygenase may well account for the indomethacin-sensitive component of carbachol effect on smooth muscle of infected animals.