Document Type : Thesis

Document Title : *Impact of inflammatory and Anti-inflammatory Mediators on Intestinal Motor Response to Infection with Schistosoma mansoni*

تأثير وسائط الالتهاب والوسائط المضادة على الاستجابة الحركية للأمعاء أثناء الإصابة بـ البلهارسيا

Document Language : Arabic

Abstract : Prostaglandin E2 is known to be the principal pro-inflammatory and inflammatory prostanoid and play an important role in communication between gastrointestinal immune system and ENS. The excitatory effects of prostaglandins on intestinal motility are mediated partially by a direct action on the enteric neurons. Somatostatin is an important neuromodulator of gastrointestinal motility and it has also been known to act as anti-inflammatory mediator during Schistosomiasis. Traditional herbal medicines such as Ferula narthex and Cymbopogon schoenanthus have been used to cure intestinal disorders in several countries including Saudi Arabia. To date, pharmacological characteristics for their effectiveness in intestinal inflammation associated with parasitic infection have not been fully determined. Our aim of the study was to investigate the role of PGE2 and EP2 receptors in the mechanisms underlying post-inflammatory changes during acute and chronic inflammation and to examine the role of pharmacological and physiological characteristics of somatostatin, Ferula narthex gum and Cymbopogon schoenanthus extracts to reduce Schistosomiasis induced hyperactivity of gastrointestinal smooth muscle that associated with severe pain during infection. Experiments were performed in Swiss male mice 4, 8 and 12-wks following infection with S. mansoni compared to uninfected control mice. Jejunal contraction was assessed using a modified Trendelenburg type preparation to study motor complexes (MCs). Data were expressed as mean ± SEM (n = 2-12) and were analysed by t- test or Mann Whitney U- test as appropriate. Infection had great effects on jejunal motility where there was a significant increase in MCs frequency reflected by increase in amplitude and decrease in interval between MCs. PGE2 (1μM) caused a significant decrease in amplitude and intervals in control, 4 and 8-wk but not 12-wk infected animals. The effect of PGE2 on MCs amplitude was more pronounced and abolished the contraction in 8 and 12-wks post-infection. EP2 agonist AH13205 (10μM) produced inhibition of MCs reflected by a significant decrease in amplitude and increase in intervals in control, 4 and 8 but not 12-wk infected animals. EP2 antagonist AH6809 (30μM) attenuated intestinal motility by a significant inhibition followed by contraction in control, 4 and 8-wks infected animals but not 12-wks post infection. EP2 receptor agonist AH13205 failed to alter the peristaltic motor activity in the presence of EP2 receptor antagonist AH6809 in control, 4, 8 and 12-wks infected jejunum. These data showed temporal differences in motor function following inflammation with parasitic infection. Somatostatin (300nM) inhibited the contractions in the jejunum in S. mansoni infected mice (4-wk post-infection). During chronic phase of infection with S. mansoni (12-wk infected mice), this inhibitory effect of somatostatin was less pronounced. Ferula narthex (3mg/ml) gum and Cymbopogon schoenanthus (10mg/ml) extract inhibited the contractions in the jejunum from uninfected control mice and from 4-wk infected mice. In 8-wk of infection with S. mansoni, the inhibitory effect of the Ferula narthex and Cymbopogon schoenanthus were more effective as compared to controls. In conclusion, PGE2 play an important role, PGE2 and EP2 receptor in regulating control and altered motility induced by parasitic infection the response to somatostatin is disturbed during chronic Schistosomiasis which might due to the disturbance of neuroregulatory circuits of enteric neurotransmission in the small intestine. The inhibitory actions of Ferula narthex and Cymbopogon schoenanthus extract on gastrointestinal motility may represent an interesting therapeutic to relieve schistosomiasis related gastrointestinal dysmotility.

Supervisor : د. فايزة بنت بكر سليمان عبده

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