Abstract

Side effects associated with nonsteroidal anti-inflammatory drugs (NSAIDs) treatment are a serious limitation of their use in anti-inflammatory therapy. These drugs show high analgesic, anti-inflammatory and antipyretic effectiveness. They are widely used, and due to the availability of many medicines without prescription, they are often abused or taken in uncontrolled doses. NSAIDs have many side effects, which are most often located in the stomach and intestines.

The enteric nervous system (ENS), which is part of the autonomic nervous system, controls most of the gastrointestinal functions. Enteric neurons are characterized by significant chemical plasticity, and the appearance of a pathological factor causes a change in the synthesis of neurotransmitters.

The aim of the study was to determine the effect of naproxen-, indomethacin- and aspirin-induced inflammation on the neurochemical expression in intramural neurons of the porcine duodenum. The experiment was carried out on 16 sexually immature gilts of the Pietrain x Duroc breed. The animals were divided into four groups: the control group (n=4) - animals were administered empty gelatin capsules, orally, for a period of 28 days; the ASA group (n=4) - animals received acetylsalicylic acid (100 mg/kg bw) *per os* for 28 days; the group INDO (n=4) - animals were given indomethacin (10 mg/kg bw) for 28 days and the N group (n=4) - animals received naproxen at a dose of 50 mg/kg bw. After this time, animals from all groups were euthanized. Then, frozen sections (14 μm thick) were prepared from the duodenum and subjected to double immunofluorescence staining. Antibodies against the neuronal marker PGP 9.5 and against vasoactive intestinal polypeptide (VIP), substance P (SP), neuronal nitric oxide synthase (nNOS), galanin (GAL), pituitary adenylate cyclase-activating polypeptide (PACAP) and cocaine- and amphetamine- regulated transcript peptide (CART) were used as primary antibodies. The secondary antibodies - Alexa Fluor 488 and 546 - were also used for staining.

The analysis of the results obtained under a fluorescence microscope showed a significant increase in the number of nNOS-, VIP-, SP-, GAL-, PACAP- and CART-immunoreactive ganglionated neurons in ASA and INDO groups. Only in animals receiving naproxen, an increase in the number of nNOS-, VIP-, CART-, GAL- and PACAP-IR neurons and a decrease in the number of SP-positive neurons in the myenteric and submucosal plexuses were noted.

The obtained results indicate the participation of enteric neurotransmitters in the neuronal response of the duodenum to inflammation induced by applied the NSAIDs administration.