CENTRAL INFLUENCE OF MGLUR RECEPTOR ANTAGONISTS ON THE HYPERALGESIC EFFECTS OF COLONAL DISTENSION IN SHEEP

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Introduction/objective: The aim of this study was to analyse the central analgesic action of L- and D,L-2-Amino-3-Phosphonopropionic acid (L-AP3 and D,L-AP3) on animal behaviour, reticulo-ruminal motility, plasma catecholamine concentration, as well as clinical symptoms of visceral pain induced by colonal wall distension (CD).

Material and methods: A 5 min CD wall was caused by an insertion of a balloon filled 150 and/or 200 ml of water. Animal preparation using stereotaxic and chirurgical methods were as prescribed previously (Kania et al., 2006). Both compounds were dissolved in 0.2 ml 0.9% NaCl and icv infused during 1 minute in the doses of 0.2, 0.4 and/or 0.8 mg (L-AP3) and 4.0, 8.0 and/or 12.0 mg (D,L-AP3) in toto, alone and 10 minutes before CD.

Results and discussion: A 5 min distension of the colonal wall, using balloon filled with 150 and/or 200 ml of water at animal body temperature, produced a significant increase in plasma CA levels, an increase in the heart rate, hyperventilation, and other clinical symptoms (inhibition of reticulo-ruminal motility, bleating, teeth grinding, prostration, urination, defecation), that may be related to pain, proportionally to the degree of CD. Intracerebroventricular administration of L- and D,L-AP3 10 min before applying CD, prevented or abolished the increase in blood plasma CA, inhibition of reticulo-ruminal contractions and behavioural symptoms provoked by CD. The colonal distension causes a general defence reactions like stress, an not just a viscero-visceral inhibitory reflex, determined on the basis of stomach motility inhibition (Brikas et al., 1993). Therefore, the nociceptive factor not only causes a viscero-visceral inhibitory mechanism but also general pain, which in the same time is a stressoric factor (Kania et al., 2009).

Nociceptive stimuli cause activation of the cortisol-catecholaminergic system, and beta-endorphins, CCK are co-released with ACTH in the CNS. The psycho-physical stimulation causes an increased secretion of both glutamate and neurokinins from the opioidergic endings (Han, 1995).

Conclusion: Both L-AP3 and D,L-AP3 as a non-specific mGluR metabotropic receptor antagonists may be recommended to treatment of visceral pain.

Keywords: mGluR antagonist, colonal hyperalgesia, sheep