Effect of leukotriene inhibitors on evolution of experimental brain contusions.

C. Voigt, C. K. Donat, W. Hartig, A. Förschler, M. Skardelly, D. Stichtenoth, T. Arendt, J. Meixensberger and M. U. Schuhmann (2012) Neuropathology and Applied Neurobiology38, 354-366 Effect of leukotriene inhibitors on evolution of experimental brain contusions Aims: Leukotriene levels increase in cerebrospinal fluid (CSF) following controlled cortical impact (CCI) injury in rats. We investigated the impact of two different leukotriene inhibitors in the CCI model on CSF leukotriene levels, brain water content (BWC), brain swelling (BS) contusion size and cellular response. Methods: 134 male Sprague Dawley rats were investigated at 4, 24 and 72 h after CCI for CSF leukotriene levels and BWC/BS, lesion size in T2-weighted magnetic resonance imaging and immunohistochemistry. Animals received vehicle, MK-886, an inhibitor of 5-lipoxygenase activating protein, or Boscari(®), a mixture of boswellic acids, acting as competitive nonredox 5-lipoxygenase inhibitors before trauma and then every 8 h until sacrifice. Results: The intracranial pressure (ICP) was unaffected by treatment. Boscari treatment reduced CSF leukotriene C4 increase by -45% at 4 h (P< 0.03) and increase of BWC and BS by 49% (P< 0.05) and -58% at 24 h. Treatment with both substances showed a reduction of lesion volume at 72 h by -21% (P< 0.01) in T(2)-weighted magnetic resonance
imaging, which was reflected in a smaller lesion area determined from a NeuN labelled section (-17% to -20%, P< 0.05). Triple immunofluorescence and Fluoro-Jade B staining showed rarefaction of neurones, glia and vasculature in the contusion core, whereas in the pericontusional zone astro- and microglia were upregulated in the presence of dying neurones. Treatment resulted in an improved survival of NeuN labelled neurones in the pericontusional cortex (+15% to +20%, P< 0.05).

Conclusions: Leukotriene inhibition should be further investigated as therapeutic option to counteract secondary growth of traumatic brain contusions and to possibly improve pericontusional neuronal survival.

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