Interleukin-1beta in synergism gabapentin with tramadol in murine model of diabetic neuropathy

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Neuropathic pain is a complication of cancer and diabetes mellitus and the most commonly used drugs in the treatment of the diabetic neuropathic pain have only limited efficacy. The aim of this study was to evaluate the role of the biomarker interleukin-1beta (IL-1ß) in the pharmacological interaction of gabapentin with tramadol in a model of diabetic neuropathic pain. CF-1 male mice, pretreated with 200 mg/kg i.p. of streptozocin (STZ), were used and at day 3 and 7 were evaluated by the hot plate test and the spinal cord level of IL-1ß was determined. Antinociceptive interaction of the coadministration i.p. of gabapentin with tramadol, in basic of the fixed the ratio 1:1 of their ED50 values alone, was ascertained by isobolographic analysis. Tramadol was 1.13 times more potent than gabapentin in saline control mice, 1.40 times in STZ mice at 3 days and 1.28 times in STZ at 7 days. The interaction between gabapentin and tramadol was synergic, with an interaction index of 0.30 and 0.22 for mice pretreated with STZ at 3 and 7 days. The combination of gabapentin with tramadol reversed the increased concentration of IL-1? induced by STZ in diabetic neuropathic mice. These findings could help clarify the mechanism of diabetic neuropathy.