EXPRESSION OF TRPV1 AND CGRP IN SPINAL PRIMARY AFFERENT NEURONS IN A RAT MODEL OF BORTEZOMIB-INDUCED PERIPHERAL NEUROPATHY TREATED WITH ANALGESICS

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Bortezomib (BTZ), a selective proteasome inhibitor, is an antitumor drug used to treat multiple myeloma. As a side effect, BTZ determines a painful peripheral neuropathy (PPN), often refractory to management. Chronic BTZ administration in female Wistar rats induced a PPN in which the development of mechanical allodynia is associated to an increase in the expression of TRPV1 and CGRP in the dorsal root ganglia (DRG) and spinal cord dorsal horn. In this study we examine the possible role of two standard analgesics, Gabapentin (Gaba) and buprenorfin (Bupre), in modulating the expression of TRPV1 and CGRP in the DRG and spinal cord of rats chronically treated with BTZ. To this aim, female Wistar rats were treated with BTZ 0.20 mg/kg, 3 times a week for 8 weeks (i.v.). Then Gaba (100 mg/kg, daily, p.o.) and Bupre (28,8 µg/kg, daily, s.c.) were orally administered in a curative schedule for 2 weeks. The expression of TRPV1 and CGRP, a neuropeptide involved in nociceptive neurotransmission, was examined in L4-L5 DRG and spinal cord segments by means of western blot (WB) and immunohistochemistry.
WB analysis did not show any statistically significant change of protein levels in DRG and spinal cord. Instead, chronic BTZ treatment followed by a 2 weeks follow-up period affected TRPV1 expression by inducing an increase in the proportion of TRPV1-like immunoreactive (LI) DRG neurons, whereas did not affect the percentage of CGRP-LI neurons. Labeled perikarya were mostly of small- and medium-size. No BTZ-induced changes in immunolabeling were appreciable in the dorsal horn of the spinal cord. Treatment with Gaba and Bupre reduced levels of TRPV1 protein in spinal cord homogenates, whereas had no effect on DRG protein levels. None of the analgesics appeared to reverse in a statistically significant way the BTZ-induced increase of labelled DRG neurons nor induced any change in the detectability of positive innervation in the spinal cord dorsal horn.