ANALGESIC EFFECT OF BACLOFEN (BETA-P-CHLOROFENIL GABA) IN EXPERIMENTAL NEUROPATHIC PAIN (Abstract). **Thesis. Fortaleza, 1995**

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Neuropathic pain is prevalent in 1% in general population. The challenge with this is bound to the difficulties in understanding its mechanisms and physiopathogenesis. This is expressed in the diversity of syndromes and therapies. Among different therapies, the baclofen has been used in only some of the pathological conditions such as trigeminal neuralgia, and more recently, in some pain syndromes of central origin. This way we aimed at defining the analgesic effect of baclofen in experimental neuropathic pain.

For this we have reproduced in 17 Wistar rats a constrictive sciatic mononeuropathy in the right hind limb as described by Bennet and Xie (1988) . As controls, two groups of 8 rats were used (sham-operated and normal animals). In all, 33 animals were followed. As parameters for the study, we selected the scratching behaviour, described in the literature as suggestive of animal chronic pain, and the measure of latency of hindlimb withdrawal to thermal stimulus of 40°C (non-nociceptive) and 46°C (nociceptive), in order to define allodynia or hyperalgesia in the experimental animals. For the pharmacological study, we used baclofen (in the doses of 1, 2, 4, and 8 mg/kg PO), vigabatrin (5 and 20 mg/kg PO) and valproic acid (15 mg/kg PO), in order to corroborate the participation of GABA system in analgesia, and naloxone (2.5 mg/kg IP) for defining a possible opioid participation in this effect. Statistically we used parametric (F Statistics of Snedecor, Tukey Test) and non-parametric (Mann-Whitney and Wilcoxon) tests. The ethical guidelines of IASP have been followed.

Our results showed a chronic significant ($p<0.05$) increase of the scratching behaviour along 4 months, and predominating in the right hindlimb.

The baclofen in the different doses exerted a significant ($p<0.05$) decrease in the scratching behaviour. This depressing effect occurs persistently with all doses as compared with the other behaviours. Moreover, the thermal tests showed the existence of allodynia and hyperalgesia in the neuropathic rats. This was reverted significantly ($p<0.01$) by effect of baclofen in the dosis of 2 mg/kg PO.

The naloxone did not succeed to revert the depressing effect of baclofen on the scratching behaviour as well as on the effect of baclofen in the thermal tests, what shows a non-participation of the opioid system in the analgesic effect of baclofen.

Other gabaergics (vigabatrin and valproic acid) were also effective in decreasing significantly ($p<0.05$) the scratching behaviour and in increasing significantly ($p<0.01$) the threshold to thermal stimulus in the neuropathic rats.

This way we conclude that the baclofen exerts an analgesic effect on experimental neuropathic pain. Besides this, we also conclude that the opioid system is not involved in its analgesic effect, and that the GABA system participates in fact in analgesia as corroborated in the results with vigabatrin and valproic acid.

KEY WORDS: **animal, neuropathic pain, chronic pain, baclofen, GABA, analgesia.**

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