

## **ANALGESIC EFFECT OF BUPRENORPHINE IN AN EXPERIMENTAL MODEL OF PAINFUL DIABETIC PERIPHERAL NEUROPATHY**

Chiorazzi Alessia (1), Carozzi Valentina (1), Canta Annalisa (1), Meregalli Cristina (1), Oggioni Norberto (1), Bianchi Roberto (2), Lombardi Raffaella (3), Camozzi Francesca (3), Lauria Giuseppe (3) and Cavaletti Guido (1).

(1) Department of Neuroscience and Biomedical Technologies, University of Milan Bicocca, Monza

(2) Pharmacologic Institute “Mario Negri”, Milan

(3) Fondazione IRCCS National Neurological Institute “Carlo Besta”, Milan

**AIM:** Diabetic peripheral neuropathy (DPN) is a complication of inadequately treated diabetes mellitus leading to sensory loss and neuropathic pain. DPN of different severity is present during in the majority of diabetic patients. Although most patients with DPN do not have pain, a clinically-relevant proportion of them complain of chronic painful symptoms that affect their quality of life, disrupt sleep, and can lead to depression. Recent advances in understanding DPN-associated pain are likely to provide significant pathophysiological insights and offer better therapies. Opioids can be effective in the management of severe neuropathic pain. Buprenorphine is a low molecular weight, lipophilic, opioid analgesic, recently available as a transdermal matrix patch formulation (Buprenorphine TDS). Recent pharmacological and clinical studies shown that buprenorphine acts not only on nociceptive and visceral pain, but also on neuropathic pain (1). Aim of this study was to evaluate through a multimodal approach the analgesic effect of buprenorphine in an experimental rat model of painful DPN.

**MATERIALS&METHODS:** Diabetes was induced in Sprague Dawley rats by a single intraperitoneal injection of streptozotocin (STZ, Sigma-Aldrich) at the dose of 60mg/kg. After 1 month, buprenorphine at doses of 7.2 ug/24h and 14.4 ug/24h for 7 days was gradually administered by implantable osmotic pumps (ALZET) in diabetic rats. General toxicity was monitored by body weight measure while neuropathic conditions were evaluated by tail nerve conduction velocity (SNCV). The behavioural tests Plantar and Dynamic Aesthesiometer (Ugo Basile instruments) were used to determine the alterations in pain perception related to pharmacologic treatment.

**RESULTS:** Diabetes induced a statistically significant reduction in body weight and SNCV ( $p < 0.001$  diabetes vs CTRL). Treatment with buprenorphine did not alter the diabetes-induced reduction in SNCV. Plantar Test and Dynamic test showed a significant diabetes-induced hypoalgesia ( $p < 0.001$  diabetes vs CTRL) and allodynia ( $p < 0.05$  diabetes vs CTRL), respectively. Both doses of buprenorphine significantly reverted ( $p < 0.05$  buprenorphine vs diabetes) the diabetes-induced allodynia up to day 7 of treatment. No buprenorphine-induced alterations in hypoalgesic state were observed.

**CONCLUSIONS:** We provide evidence of the analgesic effect of buprenorphine in an experimental model of diabetes-induced neuropathic pain. This effect was particularly evident for allodynia that is one of the most difficult to treat and discomforting symptom for patients with DPN. These results contribute to support clinical use of buprenorphine in DPN.

### **BIBLIOGRAPHY**

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