

P011 A selective phosphodiesterase 4 (PDE4) inhibitor, rolipram, blocks the cardiac noradrenergic hyperactivity observed during morphine withdrawal

A.González-Cuello, L.Sánchez, J. Hernández, ML. Vargas, MV. Milanés and ML. Laorden

*Department of Pharmacology. School of Medicine.
University of Murcia. Spain*

Previous studies have demonstrated that naloxone administration to morphine dependent rats lead to an enhancement of noradrenaline (NA) turnover in pararell with an increase in the cAMP levels in the heart (1). The up-regulation of the cAMP pathway plays an important role in the development of morphine dependence. The present study was designed to evaluate the effect of rolipram in these processes by estimating whether this PDE4 inhibitor attenuates morphine withdrawal induced changes in NA turnover and cAMP levels in right and left ventricles of rat heart. Morphine dependence was induced by s.c. implantation of morphine or placebo (control) pellets for 7 days. Animals were received rolipram (1mg/kg, i.p.) or vehicle concomitantly with pellets of morphine. On day 8, rats were given vehicle or rolipram 30 min before saline or naloxone and decapitated 90 min later. NA turnover was evaluated by high performance liquid chromatography (HPLC) with electrochemical detection. cAMP levels were studied by radioimmunoassay (RIA). When rolipram was administered it blocks the enhancement of NA turnover and the increase in cAMP levels observed in morphine-widrawn rats. The present findings indicate that rolipram inhibits the cardiac adaptative changes observed during morphine dependence throught acting at cAMP system.

(1) Milanés MV, Fuente T and Laorden ML Naunyn-Schmiedeberg's Arch. Pharmacol. 2000, 361:61-66