

Effect of ketamine on Chronic Post-ischemia Pain (CPIP) model in Sprague-Dawley rats

Chi Wai Cheung, Suryamin Liman, Kwok Fu Jacobus Ng

Department of Anaesthesiology, The University of Hong Kong, Hong Kong, Hong Kong

The mechanism for the development of Complex Regional Pain Syndrome (CRPS) is not yet well understood. The clinical features and recent studies of CRPS have suggested that a combination of exaggerated regional inflammatory responses in injury may contribute. A Chronic Post-ischemia Pain (CPIP) model of CRPS type I was built and it was suggested the pathogenesis of CRPS could be attributed to the involvement of ischemia-reperfusion injury and inflammatory response. In this study, we evaluated the effects of ketamine on CPIP model in Sprague-Dawley rats and the results were compared with that of placebo (normal saline) and positive control (methylprednisolone). A Nitrite O-ring was placed on the rats' left hindpaw after inducing anesthesia. After 3-hour ischemia period, the O-ring was cut in order to induce reperfusion. There were 3 study groups in this study and the allocation was depended on the study medication given. Ketamine (100mg/kg, group KE), methylprednisolone (30mg/kg, group MP) or normal saline (group NS) was administrated intraperitoneally immediately after reperfusion according to the study group assigned. Successful development of CPIP was defined as 30% decrease in withdrawal threshold of Von Frey (mechanical allodynia) in ipsilateral hindpaw and all the rats would be included for data analysis. After reperfusion, mortality of rats, incidence of successful CPIP development, pain responses of ipsilateral and contralateral hindpaws, and serum pro-inflammatory markers were assessed. Mortality of rats was similar among 3 study group. The successful rates of CPIP development were 55.6% in KE group, 75% in MP group and 80% in NS group, which was not statistically significant among groups. In ipsilateral hindpaw after reperfusion, rats were found to have higher thresholds for mechanical allodynia and cold allodynia in KE group than group MP and group NS (all $p < 0.05$). In contralateral hindpaw, thresholds were also higher for mechanical allodynia and cold allodynia in group KE and group MP than group NS (all $p < 0.05$). Serum pro-inflammatory markers including TNF- α and IL-2 were shown to be significantly lower at 48th hour after reperfusion in group KE and group MP than group NS (all $p < 0.05$). Both ketamine and methylprednisolone were demonstrated to reduce inflammation after reperfusion on CPIP model in SD rats but ketamine appears to offer additional analgesic benefits such as reduced mechanical allodynia and cold allodynia.