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Pharmacokinetic Interaction Study of Ketamine and Isocorynoxeine in Rat Plasma

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***SUMMARY*. Twelve Sprague-Dawley rats were randomly divided into two groups: ketamine group and ketamine combined with isocorynoxeine group ($n = 6$). The rats of two groups received a single intraperitoneal administration of 5 mg/kg ketamine, and the other group received combined intraperitoneal administration of 5 mg/kg ketamine and 15 mg/kg isocorynoxeine together. After blood sampling at different time points and processing, the concentrations of ketamine in rat plasma were determined by the established ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS) method. Chromatographic separation was achieved using a UPLC BEH C18 column (2.1 × 50 mm, 1.7 μm) with carbamazepine as an internal standard (IS). The initial mobile phase consisted of acetonitrile and water (containing 0.1% formic acid) with gradient elution. Multiple reaction monitoring (MRM) modes were utilized to conduct quantitative analysis. The sensitive, rapid and selective UPLC-MS/MS method was successfully applied to pharmacokinetic interaction study of ketamine after intraperitoneal administration. The results showed that there may be a reciprocal inhibition between ketamine and isocorynoxeine.**

RESUMEN. Doce ratas Sprague-Dawley se dividieron aleatoriamente en dos grupos: grupo de ketamina y grupo de ketamina combinada con isocorynoxeine ($n = 6$). Las ratas de dos grupos recibieron una administración intraperitoneal única de 5 mg/kg de ketamina, y el otro grupo recibió una administración intraperitoneal combinada de 5 mg/kg de ketamina y 15 mg/kg de isocorynoxeine juntos. Después del muestreo de sangre en diferentes puntos de tiempo y procesamiento, las concentraciones de ketamina en plasma de rata se determinaron mediante el método establecido de espectrometría de masas en tándem de cromatografía líquida de ultra rendimiento (UPLC-MS/MS). La separación cromatográfica se logró utilizando una columna UPLC BEH C18 (2.1 × 50 mm, 1.7 μm) con carbamazepina como patrón interno (IS). La fase móvil inicial consistió en acetonitrilo y agua (que contenía 0.1% de ácido fórmico) con gradiente de elución. Se utilizaron modos de monitoreo de reacción múltiple (MRM) para realizar análisis cuantitativos. Un método UPLC-MS/MS sensible, rápido y selectivo se aplicó con éxito al estudio de la interacción farmacocinética de ketamina después de la administración intraperitoneal. Los resultados mostraron que puede haber una inhibición recíproca entre ketamina e isocorynoxeine.

KEY WORDS: interaction, isocorynoxeine, ketamine, pharmacokinetic, UPLC-MS/MS.

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