Poster

[P27-8] P27-8: Assay and monitoring

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[P27-8-1] A sensitive LC-MS/MS method for quantification of fluticasone propionate in human plasma after intranasal administration

Hiromi Shibasaki-Hirano[1], Rena Adachi[2], Aya Yamagata[3], Ryohei Hirano[4], Akitomo Yokokawa[5], Kaori Hosoda[6], Aki Obara[7], Kazuo Ishii[8], Takashi Furuta[9] (1.Tokyo University of Pharmacy and Life Sciences, 2.Tokyo University of Pharmacy and Life Sciences, 3.Tokyo University of Pharmacy and Life Sciences, 4.Tokyo University of Pharmacy and Life Sciences, 5.Tokyo University of Pharmacy and Life Sciences, 6.Kyorin University, 7.Kyorin University, 8.Kyorin University, 9.Tokyo University of Pharmacy and Life Sciences)

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Background

Fluticasone propionate is a synthetic glucocorticoid that has been effectively used in the treatment of asthma and allergic rhinitis. The risk of adverse systemic effects from inhaled and nasal administrated corticosteroids will depend on the extent of systemic absorption. It is difficult to measure plasma concentration for pharmacokinetic analysis, since the circulation concentrations of inhaled or nasal steroid is very low. In this study, we developed a specific and sensitive analysis of fluticasone propionate using isotope dilution methodology by HPLC-tandem mass spectrometry, and applied to measure the plasma concentration of fluticasone propionate in a healthy volunteer after intranasal administration.

Methods

Plasma samples were analyzed using an Agilent 6410A Triple Quadrupole liquid chromatography-mass spectrometer. Chromatographic separation was performed on a Gemini-NX 5 μC18 110A (50 x 2 mm i.d., 5±0.3 μm) and operated at 0.2 mL/min using the following gradient of solvent mixtures (A) 0.01 M ammonium acetate containing 0.2% acetic acid and (B) methanol. Detection was performed using electron spray ionization in positive ion mode using scheduled multiple reaction monitoring (MRM). Plasma concentrations of fluticasone propionate were determined by the present LC-MS/MS method after 7 hr of intranasal administration of fluticasone propionate 100 μg in a healthy volunteer.

Results

The lower limit of detection was 0.2 pg per injection (s/n = 5), and the lower limit of quantification was 3.1 pg/mL. The calibration curve was established in the range 3~255.5 pg/mL (r = 0.9998) with fluticasone propionate-$^{2}H_{5}$ as an internal standard for the LC-MS/MS assay. The within-day reproducibilities in the amounts of fluticasone propionate determined was good agreement with the actual amount added, the relative error being −0.1 to 3.5%. The inter-assay precision was less than 1.8%. Fluticasone propionate was detected in plasma 15 min after the administration. The values of $AUC_{0\text{-}7h}$ were 20.3 pg•h/mL.

Conclusions

The present method provides a sensitive and reliable technique for the determination of fluticasone propionate in human plasma. This validated method was successfully applied to the pharmacokinetic study at the normal daily dose of nasal splay fluticasone propionate. Furthermore, we evaluate pharmacokinetics of intranasal fluticasone propionate at steady-state.

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