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利培酮渗透泵片在Beagle犬体内的药动学

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摘要

目的 液相色谱-质谱联用方法测定Beagle犬血浆中利培酮及其代谢产物9-羟基利培酮的浓度并进行Beagle犬体内的药动学研究。方法 以甲基利培酮为内标，测定血浆中利培酮及其代谢产物 9-羟基利培酮的浓度。液相分析柱: Agilent Zorbax SB- C18 (2.1 mm×30 mm, 3.5 μm)，流动相:乙腈-水-甲酸 (体积比为 60.0∶40.0∶0.1), 流速: 0.4 mL • min-1，柱温:25℃。质谱：ESI正离子模式，干燥气流速: 9 L • min-1，干燥气温度: 350 ℃，毛细管电压: 4 000 V，裂解电压: 160 V，以选择离子反应监测(SRM)方式进行检测。结果 利培酮与9-羟基利培酮的定量限均为1 μg • L-1，提取回收率均大于86%；利培酮渗透泵片和普通片血浆中利培酮的 t1/2分别为(1.83±0.61)和(0.76±0.19 h, ρmax分别为(31.37±7.68)和(179.20±28.91) nmol • L-1；tmax分别为(3.67±0.52)和(0.71±0.10) h。 9-羟基利培酮的t1/2分别为(9.92±1.75)和(5.07±0.96) h, ρmax分别为(201.65±14.61)和(470.25±69.61) nmol • L-1, tmax分别为(9.17±0.41)和(0.71±0.10) h，利培酮和9-羟基利培酮的相对生物利用度分别为(89.74±21.79)%和(98.80±16.51)%。结论 利培酮渗透泵片血药浓度平稳，可较长时间保持血药浓度。

关键词 药剂学 利培酮 9-羟基利培酮 液相色谱-质谱联用 渗透泵片

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Pharmacokinetics of risperidone osmotic pump tablet in Beagle dogs

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Abstract

Objective To measure risperidone (RSP) and its active metabolite 9-hydroxyrisperidone (9-OH-RSP) in Beagle dog plasma with a LC/MS/MS method and investigate the pharmacokinetics in Beagle dogs. Methods Methyl risperidone (MRSP) was used as the internal standard for RSP and 9-OH-RSP. The analytical column was Agilent Zorbax SB-C18(2.1 mm×30 mm,3.5 μm). A mobile phase consisting of acetonitrile and 1‰ formic acid (V∶V=60:40) was delivered at a flow rate of 0.4mL • min-1. The column temperature was 25 ℃. Mass spectra was equipped with an electrospray ionization (ESI) source in the positive ion mode. The drying gas flow rate was 9L • min-1 and the temperature was 350℃, capillary voltage was 4 000 V, clearage voltage was 160V. The mass spectrometer was operated in the selected reaction monitoring(SRM) mode. Results The limits of quantitation for both RSP and 9-OH-RSP were 1 μg • L-1, the extraction recovery was more than 86% for both substance; The main pharmacokinetic parameters of the two risperidone preparations, the osmotic pump tablets and the reference tablets, were as follows: t1/2 (1.83±0.61) and (0.76±0.19) h; ρmax (31.37±7.68) and (179.20±28.91) nmol • L-1; tmax (3.67±0.52) and (0.71±0.10) h, respectively. The main pharmacokinetic parameters of 9-hydroxyrisperidone of the two preparations were as follows: t1/2(9.92±1.75) and (5.07±0.96) h; ρmax (201.65±14.61)和(470.25±69.61) nmol • L-1; tmax (9.17±0.41) and (0.71±0.10) h, respectively. The relative bioavailability of risperidone and 9-hydroxyrisperidone were (89.74±21.79)% and (98.80±16.51)%, respectively. Conclusion Plasma concentration of risperidone osmotic pump tablets are constant and effective plasma drug concentration can be maintained for a long time.

Key words pharmaceutics risperidone 9-hydroxyrisperidone LC/MS/MS osmotic pump tablet

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