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Pharmacokinetics

药代动力学

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Preface

Pharmacokinetics, sometimes abbreviated as PK, is a branch of pharmacology dedicated to determining the fate of substances administered to a living organism. The substances of interest include any chemical xenobiotic such as: pharmaceutical drugs, pesticides, food additives, cosmetics, etc. It attempts to analyze chemical metabolism and to discover the fate of a chemical from the moment that it is administered up to the point at which it is completely eliminated from the body. Pharmacokinetics is the study of how an organism affects a drug, whereas pharmacodynamics (PD) is the study of how the drug affects the organism. Both together influence dosing, benefit, and adverse effects, as seen in PK/PD models.[1]

Pharmacokinetics describes how the body affects a specific xenobiotic/chemical after administration through the mechanisms of absorption and distribution, as well as the metabolic changes of the substance in the body (e.g. by metabolic enzymes such as cytochrome P450 or glucuronosyltransferase enzymes), and the effects and routes of excretion of the metabolites of the drug. Pharmacokinetic properties of chemicals are affected by the route of administration and the dose of administered drug. These may affect the absorption rate.

In the present book, thirty typical literatures about Pharmacokinetics published on international authoritative journals were selected to introduce the worldwide newest progress, which contains reviews or original researches on pharmaceutical care, pharmaceutics, pharmacodynamics, pharmacoepidemiology, pharmacology and Neuroimaging, etc. We hope this book can demonstrate advances in biosensor as well as give references to the researchers, students and other related people.

[1]https://en.wikipedia.org/wiki/Pharmacokinetics.

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Contents

Chapter 1

Pharmacokinetics of Ranitidine in Preterm and Term Neonates with Gastroesophageal Reflux

Ismael Lares Asseff[1], Graciela Benitez Gaucin[2], Hugo Juárez Olguín[3], Jose Antonio Godinez Nájera[1], Alejandra Toledo López[3], Gabriela Pérez Guillé[3], Fausto Zamura Torres[1]

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Abstract: Background: The aim of this study was to determine the effect of gestational age on pharmacokinetics of ranitidine in newborns with gastroesophageal reflux. **Methods**: A prospective, descriptive and pharmacokinetic study was carried out in 30 pre-term and 20 full-term babies. 3mg/kg of ranitidine was administered intravenously to all the babies and at 0.25, 0.5, 1, 2, 4, and 8h following the administration, samples of blood were drawn to assess ranitidine levels using high performance liquid chromatographic technique. **Results**: Pharmacokinetics of ranitidine had a bi-exponential behavior with a half-life elimination of (t1/2el) 2.79h, area under curve (AUC) of 1688ng/mL, volume of distribution (Vd) of 1.44L/kg, and clearance (Cl) of 5.9L/kg/h. The median plasmatic concentration in pre-terms

was 1113ng/mL and 280ng/mL in full-terms. Vd, t1/2 and Cl presented high values in preterm although the correlation of Cl with glomerular filtration in term newborns was better. Conclusions: Plasma levels of ranitidine depend on the gestational age of the newborns. However, the possible relationship between after-birth age and pharmacokinetics of the neonates as their internal organs get matured without minding their gestational background.

Keywords: Gestational Age, Full-Term, Neonates, Pre-Term, Ranitidine, Pharmacokinetics

1. Background

Ranitidine decreases gastric acid secretion and improves esophagitis. It is then fundamental to have a good knowledge of its pharmacokinetic activities so as to make the best use of it in the treatment of every patient[1]–[4]. In normal newborns and infants, several organ systems progressively get matured to culminate in the later life and progressive maturation depends on the organ system and the specific iso-enzyme involved[5][6]. In a study by Hedenström et al.,[7], on pharmacokinetics of ranitidine in adults, it was found that the use of multiple dosing scheme of ranitidine has similar parameters as the use of single dosing scheme. Its concentration, following intravenous administrations fits to a bi-exponential kinetics. In nonates, the half-life elimination is almost 2h, and it is a little more prolonged after oral administration[8]. Hepatic metabolism is one of the elimination route and this suggests that the drug has enterohepatic re-circulation for bi-exponential rate[9].

Due to the high risk of either overdosing or under-dosing in newborns, which could lead to either therapeutic failure or toxic effect, the study of pharmacokinetics of ranitidine in this group of patients is very important[1][10][11]. The absence of specific ranitidine dosing scheme for newborns has cornered physicians to use doses obtained by modifying the dosing schemes for older and mature children. The result of this is usually overdosing or sub-therapeutic dosing scheme.

In a study of pharmacokinetics of ranitidine in 27 full-term newborns without liver or kidney problems using 2.4mg/kg of ranitidine, Fontana et al.,[12], found that the half-life elimination (t1/2el) of the drug was 3.45 ± 0.31h, the total distribution volume (Vd) was 1.52 ± 0.91L/kg and the total plasmatic clearance (CL)