Abstract

Background: Protein energy malnutrition is a public health problem affecting a great number of people. Pathophysiological imbalances in malnourished individuals have a profound impact on drug pharmacokinetics. Objective: To develop an animal model of undernutrition using male Wistar rats to be used to assess, in further studies, the impact of nutritional status on the oral bioavailability and pharmacokinetics of drugs. Design: Animals were randomly assigned to one of two groups and fed different diets for 26 days: WN (well-nourished/regular diet, N = 61) and UN (under nourished/protein-calorie restricted diet, N = 72). Assessment of the animals’ nutritional status was performed taking into account serum albumin, total cholesterol level and total body weight. A kinetic model incorporating population kinetic analysis (NONMEM) was developed to analyze body weight versus time profiles in the adaptation period following administration of the two aforementioned diets. Results: Serum albumin plasma levels were lower than 2.3 g/dL in 80% (60/72) of malnourished animals at the end of the adaptation period. The range of the total serum cholesterol was similar in both groups at the end of the adaptation period. Total body weight in all cases was less than 230 g for malnourished animals and higher than 240 g for well-nourished animals. The kinetic model assayed was confirmed to be an expansion module characterized by linear weight gain and a decline module characterized by exponential weight loss, where the weight loss rate constant is an exponential function of time. The bootstrap resampling method confirmed the stability of the model eventually selected. Conclusions: The animal model developed in this study is reliable and could be of use in evaluating the impact of nutritional state on the pharmacokinetics of drugs. The proposed mathematical model allows the body weight of animals to be predicted at a given time taking into account the diet followed in the experimental period.

Keywords

Undernutrition, Rat, Animal model, Coding.