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Population pharmacokinetics of 25-hydroxyvitamin D in healthy young adults

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Key words

Vitamin D – 25-hy-
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lation pharmacokinetics
– clearance

Abstract. Objectives: The aim of our study was to develop a population pharmacokinetic (PPK) model for 25-hydroxyvitamin D clearance in a healthy young adult population in Serbia. Methods: Study sample consisted of 70 healthy young students of the Faculty of Medical Science, University of Kragujevac, Serbia, with a mean age and body mass index of 22.39 ± 1.82 years and 21.31 ± 2.69 kgm⁻², respectively. Non-linear mixed-effect modeling (NONMEM) software was used for data analysis. A validation set of 16 participants was used to estimate the predictive performance of the pharmacokinetic model. Results: In the base model (without covariates), we had parameter estimates of 0.01 L/h for apparent clearance, 0.25 L for apparent volume of distribution, while value of minimum objective function (MOF) was 383.468. The full regression model was established by estimating the effects of 12 covariates. Mean intake of vitamin D from foods (DD) and value of phosphate in serum (PHO) were covariates included in the final model, while others were excluded in this process. The estimated value in the final MOF model was 274.555. The final regression model formula was: clearance (CL) (L/h) = $0.0711 + 0.738 \times DD + 0.618 \times PHO$. Conclusions: The PPK model obtained determined clearance of 25-hydroxyvitamin D in a healthy young adult population in Serbia. Mean intake of vitamin D from foods and serum phosphate level are the most important covariates that influence value of 25-hydroxyvitamin D clearance in healthy young adults.

its important physiological role in the human body [1]. Although there are several forms of this vitamin, two are the most important: secosteroids D₂ (ergocalciferol), which is derived from ergosterol by plants, and D₃ (cholecalciferol) obtained from cholesterol in the skin under the influence of ultraviolet B (UVB) irradiation [2, 3].

The three main sources of vitamin D are food, sun exposure, and vitamin supplements [4]. Since vitamin D content in food is very limited, sunlight exposure is the most important way to achieve and maintain adequate physiological blood levels in the human body [5]. Endogenous synthesis of vitamin D in the skin is induced by UVB radiation (290 – 315 nm), and numerous studies have pointed to factors that could limit production of 25-hydroxyvitamin D from 7-dehydrocholesterol in skin: latitude, season, time of day, skin type, cloud cover and atmospheric pollution, time spent outdoors, sunscreen use, style of dressing, etc. [6].

Vitamin D could be regarded as a vitamin and as a hormone. The necessity to intake vitamin D from exogenous sources makes it a vitamin, while it acts as a hormone in the human body [5]. Reaching optimal physiological levels of vitamin D is desirable both for children, adolescents, and elderly due to role of this vitamin not only in the metabolism of calcium and phosphate, but also in the prevention of cancer, autoimmune diseases, respiratory infections, cognitive decline, diabetes, and other chronic diseases [7, 8].

Several recent studies have reported vitamin D deficiency in healthy adults living in

Introduction

Vitamin D (calciferol) has been a subject of numerous studies for many years due to

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