Population Pharmacokinetic Models for Tacrolimus in non-transplant patients: A Systematic Review

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Abstract

Several systematic reviews have been published on tacrolimus (TAC) population pharmacokinetic (PPK) modeling; however, most of them have focused on the transplant patient population. This study investigated TAC population pharmacokinetic characteristics in non-transplant patients through a systematic review of TAC population pharmacokinetic studies carried out in this patient population, with the aim of clarifying factors affecting TAC pharmacokinetic behavior and promoting individualized TAC-based treatment in non-transplant patients. The Cochrane Library, PubMed, and Embase databases, as well as Chinese databases (SinoMed, Wanfang, and China National Knowledge Infrastructure) and related references, were searched using a non-linear mixed-effects modeling approach, from the time of inception of the databases to July 2022, to identify TAC population pharmacokinetic studies modeled in non-transplant patients. Eighteen studies, all from Asian countries (China and Korea), were included in this study. Of these studies, 56% and 28% were carried out in pediatric and adult patients, respectively. Over half of the studies (56%) were conducted in patients with nephrotic syndrome. Combined medications, body weight, genetic polymorphisms, and physiological function were the most common covariates affecting TAC clearance, and variability in the apparent volume of distribution was largely explained by body weight. In addition, only 2 studies assessed the developed models through external evaluation. In non-transplanted patients, factors that affect TAC pharmacokinetics include combined medications, body weight, genetic polymorphisms, and physiological function. Recent investigations have focused mainly on Asian populations, and expanded trials that will use external evaluations for relevant model assessment are required to investigate generalizability to other ethnic populations.

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