expression may be resulted from inflammation and tubular damage.

CONFLICT OF INTEREST

None declared.

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Is a Lower Dose of Cyclosporine Required Among Iranian Kidney Transplant Recipients?

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Cyclosporine A is widely used as maintenance immunosuppressive regimen in solid organ transplantation and remains the base of immunosuppression therapy in most organ transplant patients.[1-3] Although, there is no consensus on the optimal dosage, the appropriate cyclosporine blood level is conventionally identified based on the therapeutic drug monitoring (TDM) of cyclosporine to reach the therapeutic level.[4-7] This is an important issue, because this approach is necessary to prevent allograft rejection and nephrotoxicity. Although cyclosporine dosage is routinely monitored by predose blood trough level (C0) or the 2-hour postdose level (C2),[3-7] there is poor correlation between clinical outcome and drug concentration assessed using this strategy.[1,5,7-9] On the other hand, cyclosporine can cause several side effects such as gingival overgrowth.[10]

Cyclosporine-induced gingival enlargement in Iranian kidney transplant patients seems to be prevalent; Ghafari and coworkers reported a frequency of 35% among Iranian kidney transplant recipients receiving cyclosporine.[11] Therefore, modification of the individual doses of cyclosporine by monitoring of cyclosporine blood level is crucial to avoid side effects.[4] Furthermore, C2 blood level

seems to be more likely superior to C0 blood level; higher C2 blood level is associated with fewer acute rejection episodes in the first year following kidney transplantation,[1] and C2 blood level monitoring is more accurate for prediction of graft loss in kidney transplants.[3] However, concentrations that are therapeutic after transplantation remain unclear because of the various responses of individual patients to the drug.[7] Unfortunately, side effects can also be seen at the therapeutic levels of the drug in transplant recipients.[2]

Hami and colleagues reported that C2 blood concentration is not a good predictive value for kidney allograft side effect[6]; hence, we need a reliable way to monitor cyclosporine treatment because adequate blood level of drug is required for avoidance of kidney allograft rejection.[9] The C0 level does not have a direct correlation with the side effects of cyclosporine, either, and it is not a suitable tool for dose adjustment.[6] In addition, no significant difference is observed between cyclosporine levels within acute rejection and during normal allograft function.[4] Einollahi and colleagues revealed that cyclosporine absorption, described as the C2/C0 ratio, has a considerable relationship with kidney allograft function. It is interesting that this correlation is stronger than its relationship with C0 and C2 blood levels.[8] In addition, they showed cyclosporine blood levels significantly reduced over time due to increasing the cyclosporine absorption over the time.[8] Thus , cyclosporine absorption is also useful for distinguishing the high or low cyclosporine absorbers to prevent under- or overimmunosuppression, and it can be valuable to choose optimal cyclosporine dosages in both the early and late posttransplant periods.[8] It has been revealed that African-American and nonwhite South American transplant recipients have a poor absorption profile for those drugs than Caucasians.[12]

In the current issue of the *Iranian Journal of Kidney Diseases,* Rostami and colleagues[13] showed that the cyclosporine levels for Iranian kidney transplant patients are lower compared to recommended levels for western countries.[14-17] They suggested the cyclosporine doses for Iranian kidney transplants should be adjusted according to age, sex, and donor type.[13] In a study, Einollahi and coworkers showed a relatively good outcome in kidney recipients despite apparently lower concentrations of C2 blood level compared with international consensus recommendations.[7] In addition, Pourfarziani and associates demonstrated acceptable patient and graft survival rates in patients who had lower C2 blood levels than the suggested ranges. They suggested that various ethnic populations in different parts of the world may require different target cyclosporine blood levels for the drug dose adjustment.[2] In another Iranian study, Assari and colleagues recommended that the optimal blood level of C2 may be different in various ethnic populations.[18] It seems that the current internationally recommended cyclosporine levels are also higher for other Asian ethnic kidney transplant population, such as those reported from Taiwan and Bangkok.[19,20] It is important to note that using the lower doses of cyclosporine can result in a better graft function and prevent cyclosporine nephrotoxicity as well as chronic allograft nephropathy.[21] Reduced cyclosporine exposure can be prevent other complications, including cardiovascular events, malignancies, hypertension, gingival overgrowth, etc.

Although Beiraghdar and associates showed a correlation between cyclosporine blood levels and kidney allograft function in pediatric recipients, these recipients require larger doses of cyclosporine than adults.[22] Contributing variables among pediatric kidney transplants is the variation of cyclosporine bioavailability via the intestinal length, metabolism in the gastrointestinal system, and transplant duration. It is of interest to note that the systemic clearance of cyclosporine is quite greater in the children; however, no difference is observed in the volume of distribution of drug between pediatric and adult kidney transplant patients.[22]

P-glycoprotein, a transmembrane transporter of cyclosporine, is expressed lower in women than it is in men. This could explain the sex-related differences in the pharmacokinetics of immunosuppressant drugs.[23] In addition, Nemati and colleagues suggested that genetic factors may play a role in this issue.[24] They found that human leukocyte antigen-B27 considerably correlated with a greater bioavailability of cyclosporine blood levels among kidney transplant patients; thus, recipients who express human leukocyte antigen-B27 can receive lower doses of cyclosporine to prevent its toxicity.

CONFLICT OF INTEREST

None declared.

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