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References

Systematic Review of Calcineurin Inhibitor Monitoring and Dosing Strategies in Renal Transplantation:
Notice of a New Report Funded by the Agency for Healthcare Research and Quality

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The calcineurin inhibitors (CNIs)6 tacrolimus (TAC) and cyclosporine A (CsA) are effective immunosuppressive agents for renal transplantation but require careful management to avoid toxicity. Routine therapeutic monitoring guides dosing, but uncertainty surrounds different monitoring methods and time points. Additionally, the effectiveness of strategies to reduce CNI exposure is unclear. A recent report commissioned by the Agency for Healthcare Research and Quality (AHRQ) based on research conducted by the ECRI Institute–Penn Medicine Evidence-based Practice Center to address these questions is now available (https://www.effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports). The systematic review evaluates the evidence for 3 questions. The first question compared immunoassay analysis with liquid chromatographic or mass spectrometric analytical techniques for therapeutic monitoring of CNIs. The second question examined CsA monitoring time points, and the third question evaluated alternatives to full-dose CNI regimens. The review included 105 studies.

Eleven studies addressing the analytic validity of monitoring methods suggest that chromatographic techniques more accurately and precisely measure CNI concentrations than commonly used immunoassays. However, it is unclear whether the differences are clinically meaningful. Six studies of monitoring time points do not suggest any clear clinical benefit of monitoring 2 h after the drug dose (C2) vs monitoring the trough concentration (C0), and suggest that risk of acute rejection is similar between new renal transplants monitored at C0 and those monitored at C2.

Alternatives to full-dose CNI regimens were studied in 88 trials. High-strength evidence suggests that immunosuppression with low-dose CsA or TAC, in combination with adjunctive therapies, results in lower risk of acute rejection and graft loss and improved renal function. The benefits of minimization strategies may be most significant when initiated near the time of transplant. Moderate-strength evidence suggests that conversion from a CNI to sirolimus, everolimus, or belatacept is associated with improved renal function but an increased risk of rejection, whereas high-
strength evidence suggests that withdrawal of a CNI is associated with improved renal function but an increased risk of acute rejection. Avoidance strategies of de novo use of sirolimus, everolimus, or belatacept have not been studied widely and require further research.

The review also identified important research gaps. Direct head-to-head comparisons of monitoring techniques are needed. Additionally, the ability of monitoring techniques to accurately measure low-range CNI concentrations requires further research, as CNI target therapeutic ranges have decreased over time.

The evidence base examining CNI regimens also lacks many head-to-head studies that compare different therapeutic strategies, or trials that compare low-dose to standard-dose TAC. In addition, given current practices that favor the use of TAC as a CNI, it is unclear how to interpret the available evidence, which consists largely of studies examining CsA. There is also insufficient evidence addressing the management of immunosuppression in high-risk renal transplant populations. Moreover, the follow-up periods reported in most studies are not long enough for assessing many relevant outcomes, particularly harms. Finally, better reporting of clinically important and patient-centered outcomes is needed, including measures of renal function, CNI-related toxicity, side effects, and patient adherence to immunosuppressive regimens.

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Unveiling the Right Side

An Unbiased View of Bias

Usha Anand*

Bias is an important concept in the clinical laboratory scene, it is taken or considered to be the arithmetical difference between the mean of multiple measurements, for a particular analyte; against the result from a reference method, considered as right. The inherent difference is what constitutes the systematic error; it may be quantified, but is often difficult to eliminate altogether.

The frequency distribution of the results shows a rise and a fall; with a peak in the middle, showing the average of them all. The true value of the measurand is at a distance from the mean. This gap representing the bias, on the graph can be easily seen. A gaussian type of curve, typically taking the shape of a bell; is commonly used in metrology to illustrate this point very well.

Bias may be constant throughout the measuring range, if the difference between two methods does not change;

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