IMMUNOSUPPRESSANT DRUG PROFILE 3 (LC-MS / MS)	
Cyclosporine	ug/L
Tacrolimus	ug/L

ORGAN TRANSPLANT	THERAPEUTIC RANGE OF CYCLOSPORINE A in ug/L
Kidney	1 month post transplant : 100 – 200 2-3 months post transplant : 75-150 4-5 months post transplant: 50-100 6-12 months post transplant: 25-50
Liver	290 - 525
	Toxic value : >700

KIDNEY TRANSPLANT	POST TRANSPLANT	THERAPEUTIC RANGE OF TACROLIMUS in ug/L
PEDIATRIC	0-3 months 3 -6 months 6-12 months >12 months	10-12 8-10 6-8 4-7
ADULT	0-6 months 6-12 months >12 months >5 years	8-10 6-8 4-6 3-5
	Toxic range	>20

LIVER TRANSPLANT	POST TRANSPLANT	THERAPEUTIC RANGE OF TACROLIMUS in ug/L
PEDIATRIC	0-3 months 3 -6 months >6 months	10-12 8-10 6-8
ADULT	0-3 months 3-6 months >6 months	10-12 8-10 6-8
	Toxic range	>20

Note :

i. Optimal blood levels of Cyclosporine are influenced by nature of the transplant, age and general health of the patient, co-administration of drugs, clinical findings, individual sensitivity to immunosuppressive and nephrotoxic effects of the drug, time post transplant, commercial preparation & hepatic & renal function

ii. Many drugs affect Cyclosporine blood concentration: Calcium channel blockers, Antifungal drugs & Erythromycin may prolong metabolism thus

increasing the risk of toxicity. Anticonvulsant drugs & Rifampicin may induce metabolism of Cyclosporine thus reducing bioavailability.

iii. Drug concentrations can be measured by either chromatographic (LC-MS/MS) or immunoassay (CLIA) methodologies. These two techniques are not directly interchangeable and the measured drug level depends on the methodology used. Reference ranges are different for the two methodologies. Generally CLIA has a positive bias as compared with LC-MS/MS due to cross reacting antibodies with the drug metabolites.

iv. Test conducted on whole blood.

Comments

LC-MS/MS is considered the most sensitive, specific and precise technology for monitoring immunosuppressants. Therapeutic drug monitoring (TDM) is commonly used to help maintain drug levels within the concentration range in which the drug exerts its clinical effect with minimal adverse reactions.

Cyclosporine provides maintenance immunosuppression by inhibition of the activation of T lymphocytes via a multifaceted mechanism. It is slowly absorbed and reaches peak concentrations in 4-6 hours. The elimination profile of Cyclosporine is biphasic, early elimination phase with half life ranging from 3-7 hours followed by a slower elimination phase with half life ranging 18-25 hours. Maximum suppression with Cyclosporine occurs during the first 24 hours of antigen stimulation by the allograft. Thus it must be administered in the early phase of the immune response to achieve success of transplantation.

Tacrolimus is a potent immunosuppressant approved for prophylaxis of organ rejection in patients receiving allogeneic liver transplants. It has also been used effectively in other solid organ transplant patients like kidney transplant for prevention of graft versus host disease as well as in pancreatic islet transplantation. It exerts immunosuppressive effect following the formation of a complex with immunophilins. It's absorption from small intestine is highly variable ranging from 4-93% and changes with time following transplant surgery. Even the elimination half life of Tacrolimus is variable being 12 hours in liver transplant patients and 19 hours in renal transplant patients.