IMMUNOSUPPRESSANT DRUG PROFILE 2 (LC-MS / MS)	
Cyclosporine	ug/L
Sirolimus	ug/L

Interpretation

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

ORGAN TRANSPLANT	THERAPEUTIC RANGE OF SIROLIMUS in ug/L
Kidney (in combination with Cyclosporine A)	4 -12
Liver	12 -20
	Toxic Value: >25

Note :

1. 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

2. 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.

2. 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.

1. 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.

Sirolimus acts by suppressing cytokine driven T lymphocyte proliferation thereby inhibiting progression from G1 to S phase of the cell cycle. It is rapidly absorbed from the GI tract reaching peak concentration in whole blood in about 2 hours. It does not appear to be nephrotoxic.

Indications for testing

- Immunosuppressant dose optimization
- Failure to respond to immuosuppressants
- Signs or Symptoms consistent with inadequate or excessive immunosuppression
- Changes to concomitant medications or other variables that affect pharmacokinetics