MAYO CLINIC LABORATORIES

Test Definition: PNYA

Phenytoin, Total, Serum

Overview

Useful For

Monitoring for appropriate therapeutic concentration

Assessing compliance or toxicity

Method Name

Kinetic Interaction of Microparticles in a Solution (KIMS)

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Collection Container/Tube: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial within 2 hours of collection.

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
-Neurology Specialty Testing Client Test Request (T732)
-Therapeutics Test Request (T831)

Specimen Minimum Volume

0.25 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	7 days	

	Ambient	7 days	
	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Phenytoin is the drug of choice to treat and prevent tonic-clonic and psychomotor seizures. If phenytoin alone will not prevent seizure activity, coadministration with phenobarbital is usually effective.

Initial therapy with phenytoin is started at doses of 100 to 300 mg/day for adults or 4 mg/kg/day for children. Because absorption is variable and the drug exhibits zero-order (nonlinear) kinetics, dose must be adjusted within 5 days using blood concentration to guide therapy. Oral bioavailability ranges from 80% to 95% and is diet-dependent.

Phenytoin exhibits zero-order pharmacokinetics; the rate of clearance of the drug is dependent upon the concentration of drug present. Therefore, phenytoin does not have a classical half-life like other drugs, since it varies with blood concentration. At a blood concentration of 15 mcg/mL, approximately half the drug in the patient's body will be eliminated in 20 hours. As the blood concentration drops, the rate at which phenytoin is excreted increases.

Phenytoin has a volume of distribution of 0.65 L/kg, and is highly protein bound (90%), mostly to albumin.

Some drug side-effects occur in the therapeutic range; these include gingival hyperplasia, hyperglycemia, and skin rash.

Phenytoin pharmacokinetics are significantly affected by a number of other drugs. As noted above, phenytoin and phenobarbital are frequently coadministered. Induction of the cytochrome P450 enzyme system by phenobarbital will increase the rate at which phenytoin is metabolized and cleared. At steady-state, enzyme induction will increase the rate of clearance of phenytoin such that the dose must be increased approximately 30% to maintain therapeutic levels.

Uremia has a similar effect on phenytoin protein binding. In uremia, by-products of normal metabolism accumulate and bind to albumin, displacing phenytoin, which causes an increase in the free (active) fraction.

Concurrent use of phenytoin and valproic acid (another frequently used antiepileptic) may result in altered valproic acid levels and/or altered phenytoin levels. Due to the complex situation involving displacement of protein-bound phenytoin and inhibition of phenytoin metabolism, as well as the potential for decreased valproic acid concentrations, patients should be monitored for both phenytoin toxicity and therapeutic efficacy. Free phenytoin levels should be measured to provide the most accurate assessment of phenytoin activity early in therapy. At steady-state, free phenytoin and free valproic acid concentrations should be normalized.

The free phenytoin level is the best indicator of adequate therapy in renal failure.

In renal failure, the opportunity for the free phenytoin fraction to be cleared is significantly reduced. The end result is that both the total and free concentration of phenytoin increase, with the free concentration increasing faster than the total. Dosage must be reduced to avoid toxicity. Accordingly, the free phenytoin level is the best indicator of adequate therapy in renal failure.

Toxicity is a constant possibility because of the manner in which phenytoin is metabolized. Small increases in dose can lead to very large increases in blood concentration, resulting in early signs of toxicity such as nystagmus, ataxia, and dysarthria. Severe toxicity occurs when the blood concentration is above 30 mcg/mL and is typified by tremor, hyperreflexia, and lethargy. The outcome of phenytoin toxicity is not as serious as phenobarbital because phenytoin is not a central nervous system sedative.

Reference Values

Therapeutic: 10.0-20.0 mcg/mL
Critical value: > or =30.0 mcg/mL

Interpretation

Dose should be adjusted to achieve steady-state total phenytoin concentrations between 10.0 and 20.0 mcg/mL.

In patients with renal failure, total phenytoin is likely to be less than the therapeutic range of 10.0 to 20.0 mcg/mL. Severe toxicity occurs when the total blood concentration exceeds 30.0 mcg/mL.

Cautions

No significant cautionary statements

Clinical Reference

1. Richens A: Clinical pharmacokinetics of phenytoin. Clin Pharmacokinet 1979;4:153-169
2. Moyer TP: Therapeutic drug monitoring. In Tietz Textbook of Clinical Chemistry. Fourth edition. Edited by CA Burtis, ER Ashwood. WB Saunders Company, Philadelphia, 2005, pp 1237-1285

Performance

Method Description

The assay is based on the kinetic interaction of microparticles in a solution (KIMS). Phenytoin antibody is covalently coupled to microparticles and the drug derivative is linked to a macromolecule. The kinetic interaction of microparticles in solutions is induced by binding of drug-conjugate to the antibody on the microparticles and is inhibited by the presence of phenytoin in the sample. A competitive reaction takes place between the drug conjugate and phenytoin in the serum sample for binding to the phenytoin antibody on the microparticles. The resulting kinetic interaction of microparticles is indirectly proportional to the amount of drug present in the sample.(Package insert: ONLINE TDM Phenytoin reagent; Roche Diagnostics; 09/2022)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

Same day/1 day

Specimen Retention Time

1 week

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

80185

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PNYA	Phenytoin, Total, S	3968-5

Result ID	Test Result Name	Result LOINC® Value
PNYA	Phenytoin, Total, S	3968-5