# Serum Phenobarbitone Levels in Neonates with Seizures: Some Clarifications

We read with interest the observational study by Wasim, *et al*. [1] and seek the following clarifications:

1. It is not clear how clinical seizures were diagnosed and by whom, as the sensitivity of clinical assessment is just about 50%.
2. Exclusion of babies who needed ventilation may make the results erroneous as the respiratory depression induced by phenobarbitone itself may have caused such a need.
3. In practice, it is very difficult to achieve a rate of infusion of 1 mg/kg/min for a 20 min duration. How did the authors achieve the same?
4. Why did authors measure serum levels immediately after the infusion? It is usually recommended to measure peak level after 2 hours [2].
5. In the abstract, the authors seem to make a potentially dangerous generalization that drug level monitoring is unnecessary. If so, how do we diagnose the CNS depression and other adverse effects related to phenobarbitone toxicity?
6. The number of children having seizures related to hypoxic ischemic encephalopathy is not quoted.

**A. SHASHIDHAR**
*Department of Neonatology,*
*St. John's Medical College, Bangalore ,*
*Karnataka, India.*
*shashiishere@gmail.com*

**REFERENCES**

1. Wasim S, Upadhyay A, Roy M, Saxena P, Chillar N. Serum phenobarbitone levels in term and near-term neonates with seizures. Indian Pediatr. 2016;53:388-90.
2. Koren G. Therapeutic drug monitoring principles in the neonate. Clin Chem. 1997;43:222-7.

## AUTHORS' REPLY

We are thankful to the reader for the opportunity to provide clarifications regarding the paper [1].

1. Clinical seizures were diagnosed by the two residents who were trained for identifying the neonatal seizures as per standard criteria [2].
2. We excluded babies who required ventilation right at admission and not those who require ventilation later in course of admission after enrolment in study. This was done to reduce the attrition rate from the study as extramural babies coming to us in very moribund condition had high likelihood of death without completion of study protocol.
3. It was not at all difficult to follow this schedule of phenobarbitone administration with the help of syringe pump.
4. Time for peak concentration of phenobarbitone is 0.5-4 hours. The study did not measure the peak serum levels of phenobarbitone. Many neonates reached therapeutic level immediately after infusion. The mean serum phenobarbitone level achieved at 20 minutes in our study was comparable to that at 12 hours. So, it can be presumed that there will be no difference between 20 minutes and other time intervals like 30 minutes or 2 hours as well. Some other studies have also measured the serum phenobarbitone levels at 20 minutes [3,4].
5. As the seizure control in our study was independent of serum levels of phenobarbitone, serum level monitoring may not be essential in most cases who require one or two doses of phenobarbitone. We recommend serum level monitoring in cases where we suspect side effects of this drug, or if multiple doses have been given (cumulative loading dose more than 30 mg/kg). We also need to monitor drug levels in case multiple drugs are used for seizure control as one may unpredictably increase or decrease the drug levels of the other drug.
6. Sixty-nine percent of the seizures were related to hypoxic ischemic encephalopathy.

**PRIYANKA GUPTA AND *AMIT UPADHYAY**
*Department of Pediatrics*
*LLRM Medical College, Meerut, Uttar Pradesh, India.*
**au.llrm@gmail.com*

**REFERENCE**

1. Wasim S, Upadhyay A, Roy M, Saxena P, Chillar N. Serum phenobarbitone levels in neonatal seizures in term and near-term babies. Indian Pediatr. 2016;53:388-90.
2. Volpe JJ. Neonatal Seizures. *In:* Neurology of the Newborn, 5th ed. Philadelphia: WB Saunders Elsevier: 2008. *p* 211-5.
3. Lockman LA, Kriel R, Zaske D, Thompson T, Virnig N. Phenobarbital dosage for control of neonatal seizures. Neurology. 1979;29:1445-9.
4. Ali H, AytugAtici. Single enteral loading dose of phenobarbital for achieving its therapeutic serum levels in neonates. Croat Med J. 2010;51:215-8.