

## SHORT COMMUNICATION

## Measurement of Blood Phenobarbital Concentration in Newborns Admitted to the NICU Of Imam Reza Hospital and receiving the drug via Intravenous Mode

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## **Abstract**

Introduction: Newborns may be treated with phenobarbital for many reasons. Because in each region, depending on different races and genetic factors, different pharmacokinetic conditions govern the drug. It is essential to control blood levels of certain drugs, especially phenobarbital, and maintain these levels during treatment. In this study, we measure the level of phenobarbital in newborns who receive intravenous.

*Methods:* In this study, venous blood was collected from 50 neonates who received intravenous phenobarbital at a loading dose of 20 mg/kg weight, and at least, three days had passed since the maintenance dose of 5 mg/kg body weight in 24 hours, and sent to the laboratory. Phenobarbital blood levels were measured, and the results were analyzed descriptively.

**Results:** In this study, the average weight of newborns in two groups was  $9.93 \pm 2.58$  kg. The mean blood concentration of phenobarbital, three days after starting the maintenance dose in the group of infants weighing more than 2.5 kg was  $3.33 \pm 9.1$  micrograms/liter, in the group of infants weighing less than 2 kg. and half a kilogram or LBW was  $5.9 \pm 9.5$  micrograms/liter, and in the group weighing less than 1.5 kg VLBW was  $14.4 \pm 15.46$  micrograms/liter. There was no significant difference between case and control group (p>0.05). Three days after starting the maintenance dose in all three groups, the mean blood phenobarbital concentration was  $9.86 \pm 0.86$  micrograms/liter.

Conclusion: Blood phenobarbital levels in our newborns are below therapeutic levels at day two, so phenobarbital levels should be evaluated.

Keywords: Newborn, Phenobarbital, Drug

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Phenobarbital can be used for anti-seizure management, treatment for status epilepticus, insomnia, as well as benzodiazepine and alcohol withdrawal treatment. This medication is used alone or with other medications to control seizures. Phenobarbitalis used to treat infants (ages 0-1 year) with any type of seizure disorder, and other children with generalized, partialor febrile seizures. It is also used for the treatment of status epilepticus (seizures lasting greater than 15 minutes). Phenobarbital belongs to a class of drugs known as barbiturate anticonvulsants/hypnotics. It works by controlling the abnormal electrical activity in the brain that occurs during a seizure. Take this medication by mouth with or without food as directed by your doctor, usually once daily at bedtime for seizure control. Dosage is based on your medical condition, phenobarbital blood levels, and response to treatment. The dosage in children may also be based on weight. This medication works best when the amount of drug in your body is kept at a constant level (1).

Phenobarbital is one of the oldest anticonvulsants and sedative-hypnotics (1) and is widely used in treating many diseases, especially in neonates, including in treating direct hyperbilirubinemia. It is also used in infants and treating Withdrawal syndrome (2). Its intravenous form is used in neonates as 15 to 20 milligrams per kilogram (at a rate of one milligram per kilogram per minute) as a loading dose (Exeta Limit 40 mg per kilogram) and as a maintenance dose. from 3 to 5 mg. per kg every 24 hours is recommended (3). In particular, phenobarbital is one of the drugs that, due to large differences in drug pharmacokinetics in the neonatal age group, requires control of serum drug concentrations during treatment (2, 6). Because it is difficult to monitor drug concentrations through blood sampling in the pediatric and neonatal age groups, various methods have been proposed to facilitate this, such as using saliva to monitor drug levels (18) or using DBS.

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The findings showed that because infants may be treated with phenobarbital for various reasons, and since each region is based on different races and different genetic factors, different pharmacokinetic conditions govern the drug. The blood level of this drug in our patients is lower than the therapeutic level. More studies should be done.

## **REFERENCES**

- Lee D C, Ferguson K L sedative hypnotics Nelson LS Lewin N A, Howland M A GoldFrank' Toxicologic Emergencies 9th ed McGraw Hill 2011; 1064-1065
- Dawodu T, Douma CE, Patnode R, Common neonatal intensive care unit medication guidelines, Cloherty JP Erchenwald EC Stark AR Manual of neonatal care 6th ed Wolter Kluwer Lippincott. Williams Wilkins 2008; 706
- 3. Lee C, Custer JW Rau RE. Drug doses Custer JW Rau RE the Harriet Lane handbook 18ed Mosby Elsevier 2009; 944
- Neville K A,Leeder J S Pediatric Pharmacogeneticns Pharmacogenomics and Pharmacoproteomics .KliegmanRM Stanton B F, Geme JVST Nelson Textbook of Pediatrics 19th ed elsevier saunders 2011;250
- Lobo MG, Pinheiro SM, Castro JG, Momenté VG, Pranchevicius MC. Adverse drug reaction monitoring: support for pharmacovigilance at a tertiary care hospital in Northern Brazil. BMC Pharmacol Toxicol. 2013 Jan 8;14:5. doi: 10.1186/2050-6511-14-5.
- 6. Pippenger CE, Rosen Phenobarbital plasma levels in neonates TS.Clin Perinatol. 1975 Mar;2(1):111-5.
- Karel A, Brian J; Anker VD, John N et al Clearance in Preterm Neonates: Relation to Prenatal growth Home June 2007; -Volume 29 - Issue 3
- 8. Yukawa M, Yukawa E, Suematsu F, Takiguchi T, Ikeda H, Aki H, Mimemoto M. Population pharmacokinetics of phenobarbital by mixed effect modelling using routine clinical pharmacokinetic data in Japanese neonates and infants: an update. J Clin Pharm Ther. 2011 Dec;36(6):704-10

- Pitlick W, Painter M, Pippenger C. Phenobarbital pharmacokinetics in neonates. Clin Pharmacol Ther. 1978 Mar; 23(3):346-50.
- 10. Heimann G, Gladtke E. Pharmacokinetics of phenobarbital in childhood. Eur J Clin Pharmacol. 1977; 12:305–310.
- Pitlick W, Painter M, Pippenger C. Phenobarbital pharmacokinetics in neonates. Clin Pharmacol Ther. 1978; 23:346–350.
- 12. Fischer JH, Lockman LA, Zaske D, et al. Phenobarbital maintenance dose requirements in treating neonatal seizures. Neurology. 1981; 31: 1042–1044.
- Minagawa K, Miura H, Chiba K, et al. Pharmacokinetics and relative bioavailability of intramuscular phenobarbital sodium or acid in infants. Pediatr Pharmacol (New York). 1981; 1:279– 289
- 14. Grasela TH Jr, Donn SM. Neonatal population pharmacokinetics of phenobarbital derived from routine clinical data. Dev Pharmacol Ther. 1985; 8:374–383.
- Touw DJ, Graafland O, Cranendonk A, et al. Clinical pharmacokinetics of phenobarbital in neonates. Eur J Pharm Sci. 2000; 12:111–116.
- Kokwaro GO, Ogutu BR, Muchohi SN, et al. Pharmacokinetics and clinical effect of phenobarbital in children with severe falciparum malaria and convulsions. Br J Clin Pharmacol. 2003;56:453–457
- Offie Porat Soldin\* and Steven J. Soldin† Review: Therapeutic Drug Monitoring in Pediatrics February 2002 - Volume 24 -Issue 1 - pp 9-14
- Koren G Salivary excretion of drugs in children: theoretical and practical issues in therapeutic drug monitoring. Developmental Pharmacology and Therapeutics [1992, 19(4):161-177]
- Edelbroek, Peter M PhD\*; Heijden, Jacques van der BSc†; Stolk, Leo M L PhD† Dried Blood Spot Methods in Therapeutic Drug Monitoring: Methods, Assays, and Pitfalls June 2009 -Volume 31 - Issue 3 - pp 327-336