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Exposure to excess phenobarbital negatively influences the osteogenesis of chick embryos

Yu Yan Jinan University, China

Phenobarbital is an antiepileptic drug that is widely used to treat epilepsy in a clinical setting. However, a long term of phenobarbital administration in pregnant women may produce side effects on embryonic skeletogenesis. In this study, we aim to investigate the mechanism by which phenobarbital treatment induces developmental defects in long bones. We first observed that phenobarbital treatment decreased chondrogenesis and inhibited the proliferation of chondrocytes in chick embryos. Phenobarbital treatment also suppressed mineralization in both *in vivo* and *in vitro* long bone models. Next, we established that phenobarbital treatment delayed blood vessel invasion in a cartilage template, and this finding was supported by the down-regulation of vascular endothelial growth factor in the hypertrophic zone following phenobarbital treatment. Phenobarbital treatment inhibited tube formation and the migration of human umbilical vein endothelial cells. In addition, it impaired angiogenesis in chick yolk sac membrane model and chorioallantoic membrane model. In summary, phenobarbital exposure led to shortened lengths of long bones during embryogenesis, which might result from inhibiting mesenchyme differentiation, chondrocyte proliferation, and delaying mineralization by impairing vascular invasion.

283329554@qq.com

Efficacy of current antibiotic regimens for neonatal sepsis at a tertiary hospital, January 1, 2000 to December 31, 2015: Pathogens and susceptibility, demographic profile, clinical manifestations and outcome, morbidity and mortality rate

Anne Melva V Meliton and Robert Dennis J Garcia Makati Medical Center, Philippines

Necessary and the pathogene is necessary to determine if an antimicrobial upgrade is necessary. Although, Piperacillin-tazobactam has been favored for late-onset sepsis in the unit in the last 15 years, more septic neonates ended treatment on a Carbapenem. There was no growth of ESBL *E. coli* or *Klebsiella pneumoniae* in blood isolates in spite of 15 years of current antimicrobial usage practices. A regimen of Cefuroxime and Amikacin for early-onset sepsis will miss a minority of pathogens while a Carbapenem or Piperacillin-tazobactam, with or without Amikacin, is still effective for late-onset sepsis. Vancomycin should be considered to be added in late-onset sepsis, if Staphylococcal disease is suspected.

amvmeliton@gmail.com