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Opinion
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Penicillamine - Neuroprotection against Neonatal Brain Injuries

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Keywords

D-penicillamine in the neonatal period; Autism spectrum disorders; Attention-deficit/hyperactivity disorder; Neuroprotection

Opinion

The eminent article Gale et al. [1]-I have found it during net-searching, has encouraged me to write this letter.

D-Penicillamine (D-PA) was first used in neonates for the treatment of Hyperbilirubinemia (NHBI). During this time there was a significantly low incidence of retrolental fibroplasia (RLF-now it is retinopathy of prematurity-ROP) in the infants treated with D-PA. Later, these studies were replicated in other institutes in Hungary, Poland, USA, India and Mexico. It is important to note that there was no intolerance or short-term or long-term toxicity of the medication, in spite of the fact that D-PA was used 10 to 20 times higher doses in the newborn period than those in adult. Furthermore, we have demonstrated a new concept in the etiology of Bilirubin Induced Neurologic Dysfunction (BIND) and highlighted the role of D-PA [2]. Unconjugated Bilirubin (UCB) i.e., has a high affinity for the basal ganglia. Furthermore, immaturity of the blood brain barrier also contributes to the development of BIND. Heavy metal ions, especially copper and iron play a pivotal role in the pathogenesis of neurodegenerative diseases including BIND, having impact on both protein structure (misfolding) and oxidative stress. Our recently published case report and other healthy and highly educated patients' (they are now 28 to 42 years old) follow-up suggest that D-PA administration to the newborn infants may have significant neuroprotective effects in cases jeopardized by BIND or Retinopathy of Prematurity (ROP). In addition, it was our privilege to follow a number of children who are now adults, including sons and daughters of our relatives, colleagues and close friends. They are now highly educated persons working in health care (mostly as physicians), bank, computer, and building industry, etc. Copper dyshomeostasis and oxidative stress have also been concerned in neurodegenerative/Neurodevelopmental Disorders (NDs) such as Autism Spectrum Disorders (ASD) or Attention Deficit/Hyperactivity Disorder (ADHD) [3]. Our recommendation: all newborns should be screened for ASD, particularly the premature babies and infants suffering from NHBI. These conditions significantly increase the prevalence of NDs, including ASD and ADHD. Although the 24 hour urine copper test is inconsistent in the neonatal period, the Penicillamine challenge test may be useful in the detection of higher copper in the urine [4]. For those children who are voiding copper more than usually in the given institutes or laboratories, high doses D-PA therapy is necessary for 2 to 3 weeks. Our concept was conceived because of long-term follow up (3 to 40 years) we found only 1 ASD in the children and adults who were treated with D-PA in their neonatal period (N=550 patients so far ["New prevalence numbers for 2014, 1 in 45 US children have autism"]) [5]. Our 30 years old male patient was born as a premature infant and had a serious hyperbilirubinemia. He was treated with D-PA without success, because exchange transfusion was necessary to perform [3].

References

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