EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 01
449-450
Year: 2017

VALPROATE INDUCED THROMBOCYTOPENIA AND RENAL DYSFUNCTION: CASE REPORT

Kundan Mittal*, Poonam Mehta, H. K. Aggarwal and Anindya Mittal,

[1]Professor in Pediatric and I/c Intensive Care
[2]Assistant Professor Pediatrics
[3]Senior Professor Medicine and Nephrology
[4]M.B.B.S. (Std)
Pt. B. D. Sharma, PGIMS, Rohtak, Haryana India.

Corresponding Author: Dr. Kundan Mittal
Professor in Pediatric and I/c Intensive Care.

Article Received on 01/11/2016 **Article Revised on 22/11/2016** **Article Accepted on 12/12/2016**

ABSTRACT
Valproate acid (2-propylpentanoic acid; VPA) is a branched-chain carboxylic is one of the most common drug used in management of epilepsy. The major side effects known are hepatic dysfunction, thrombocytopenia and renal tubular injury. Although most cases result from overdose and death is rare event.

KEY WORDS: Valproic acid (VPA).

Case History

Two and half year-old child, a known case of mental retardation (full term vaginal delivery, history of birth asphyxia and seizures present) with refractory seizures brought with complaint of fever, cough, cold, decrease oral acceptance since 3 days and respiratory distress and decreased urine output for the last one day. On examination, child was febrile with heart rate of 120/min, respiratory rate of 56/min, oxygen saturation of 90% with intercostal and subcostal retractions. Child was on antiepileptic drugs (valproate 45mg/kg since 6month of age). Child was admitted in pediatric intensive care unit with a presumptive diagnosis of pneumonia and severe respiratory distress and put on intravenous fluid, antibiotics (ceftriaxone) and oxygen therapy. Initial investigation revealed hemoglobin of 9gm/dl, total leucocyte counts 2500/mm^3, polymorphs 80%, lymphocytes 18%, platelet count one lakh/mm^3, blood urea 217mg/dL and serum creatinine 2mg/dL. Chest radiography showed features of aspiration pneumonia. On second day of admission child had bleeding from gums and hematuria. Child also developed progressive thrombocytopenia (platelet count 20000/ mm^3). Due to worsening of respiratory distress and pulmonary bleed child was put on mechanical ventilation. As the patients was having thrombocytopenia a possibility of valproate induced thrombocytopenia was kept and valproate was stopped and phenytoin was started and serum valproate level were sent. MRI brain revealed sequelae of hypoxic ischemic insult and EEG suggested generalized seizure disorder. Renal function improved (blood urea decreased to 67mg/dL and later on came to be normal) with improvement in urine output and platelet count. Serum valproate level came to be high that is 250mg/L (therapeutic range 50-100mg/L). Child improved clinically and was discharged on phenytoin and levatiracetam. Similar findings were observed in another 4 years child with mental retardation and refractory seizure.

DISCUSSION

Sodium Valproate is commonly used as a major drug for the treatment of various types of epilepsy. Major adverse effects include hepatic and pancreatic dysfunction, thrombocytopenia, hyperammonemia and weight gain. Oxidative stress has been proven to be involved in VPA-induced toxicity. Earlier hyperammonemia was the only renal side effects but now there have been various case reports of renal tubular injury due to valproate toxicity leading to development of Fanconi syndrome[1-5]. Recent evidence suggests that oxidative stress caused by free radicals in kidney cells contributes to the pathogenesis of VPA-induced nephrotoxicity. The levels of oxidative stress markers, lipid peroxidation (LPO), and protein carbonyl (PC) content were significantly elevated. Valproate leads to a significant increase in reduced glutathione (GSH) and non-proteinthiol level (NP-SH). VPA exposure altered the activities of glutathione metabolizing enzymes such as glutathione-S-transferase, glutathione peroxidase, and glutathione reductase and leads to increased secretion of N-acetyl-β-d-glucosaminidase (NAG) in the urine which is a marker of renal tubular injury[6]. However there have been no case reports of valproate induced renal

dysfunction leading to uremia and increase creatinine levels. There has been only one case of acute overdosing of sodium valproate in a child who presented with coma, seizures and anuria and the progressive renal insufficiency was attributed to rhabdomyolysis and myoglobinuria[7].

In contrast to our case there was one study that demonstrate that VPA has a beneficial effect on the development of proteinuria and the progression of glomerulosclerosis in the experimental Adriamycin nephropathy model[8]. The mechanism explained was that VPA halts glomerulosclerosis through inhibition of podocyte detachment, apoptosis, and proliferation. Hence still the effect on valproate on renal functions is not clear and studies are required to confirm the effects.

CONCLUSION

Valproate therapy can cause deranged blood urea and creatinine levels apart from hyperammonemia and renal tubular injury.

REFERENCES

1. Nephroprotective activities of quercetin with potential relevance to oxidative stress induced by valproic acid. Protoplasma. 2015 Jan; 252(1): 209-17.
2. Altunbasak S, Yıldız D, Anarat A, Burgut HR Renal tubular dysfunction in epileptic children on valproic acid therapy. Pediatr Nephrol 2001; 16: 256–259.
3. Endo A, Fujita Y, Fuchigami T, Takahashi S, Mugishima H. Fanconi syndrome caused by valproic acid. Pediatr Neurol 2010; 42: 287–290.
4. Knights MJ, Finlay E. The effects of sodium valproate on the renal function of children with epilepsy Pediatr Nephrol 2014 Jul; 29(7): 1131-8.
5. Raza M, Al-Bekairi AM, Ageel AM, Qureshi S. Biochemical basis of sodium valproate hepatotoxicity and renal tubular disorder: time dependence of peroxidative injury. Pharmacol Res. 1997 Feb; 35(2): 153-7.
6. Tseng CL, Wang PJ, Tsau YK, Lin MY, Shen YZ Urinary N-acetyl-beta-glucosaminidase (NAG) in children receiving antiepileptic drugs. Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi 1992; 33: 251–256.
7. Roodhooft AM, Van Dam K, Haentjens D, Verpooten GA, Van Acker KJ. Acute sodium valproate intoxication: occurrence of renal failure and treatment with haemoperfusion-haemodialysis. Eur J Pediatr. 1990 Feb; 149(5): 363-4.
8. Van Beneden K, Geers C, Pauwels M, Mannaerts I, Verbeelen D, Van Grunsven LA et al Valproic Acid Attenuates Proteinuria and Kidney Injury J Am Soc Nephrol. 2011 Oct; 22(10): 1863–1875.