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Pyridoxine Toxicity in Pediatric Patient with ESRD on Peritoneal Dialysis. Case Report

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Abstract

Pyridoxine induced toxicity was first described in 1984 in 58 years old female patient who used megadose as prescribed by her physician to treat carpal tunnel syndrome. Later on, couple of case report also reported different forms of neurosensory toxicity in adult patients on high doses and/or long-term therapy of pyridoxine. We present the first case of pyridoxine toxicity in pediatric patient received therapeutic dose of pyridoxine of 1 mg/kg/day once daily who presented with low blood pressure, headache and hypersomnia.

Index terms— pyridoxine, children, toxicity.

1 Possibility of pyridoxine induced neurotoxicity

was considered yet pyridoxine level couldn't be sent because of lack of availability. Therefore, child was admitted for observation and pyridoxine was put on hold.

On Day 1 of admission, child was clinically stable; nurses and parents were instructed clearly to not administer pyridoxine to the child. Neurology team was involved to evaluate the child, they have concluded that symptoms go with peripheral neuropathy, looking into the clinical and laboratory data the likely cause is pyridoxine Infectious disease team was consulted for dose adjustment; the dose was decreased to half of the initial dose for his weight and child was discharged on 10 mg OD dose with close follow-up.

He was seen after two weeks in infectious disease clinic and parents reported significant improvement of his symptoms, yet he is still not at his baseline. Month later, child was readmitted in general ward under his primary team for treatment of peritonitis; mother mentioned that child still suffering from increase sleepiness and lethargy and that they haven't completely resolved even after reducing medication to half. After discussion with his primary team and infectious disease team, pyridoxine was stopped completely with close follow up. On subsequent out patient visit; his symptoms improved dramatically and he continued on isoniazid alone.

2 II.

3 Discussion

Kidney transplantation is the best option of treatment for children with end stage kidney disease. Mantoux test is considered as part of pretransplant work up.

Our patient was diagnosed to have latent disease based on positive tuberculin skin test and negative chest X-ray in asymptomatic patient. He was started on treatment with INH and pyridoxine regimen.

Vitamin B6 is a water-soluble vitamin which present in mainly 3 natural forms, commonly used in clinical practice is pyridoxine [6,21].

Vitamin B6 is absorbed into the body and then converted to pyridoxal 59-phosphate -it's active form-(PLP). It acts as an enzyme co-factor and or regulator, facilitating different cellular function. It's essential in amino acid metabolism, energy-generating pathways, immune function as well as steroid synthesis [9, **??**] Later on, couple of case report also reported different forms of neurosensory toxicity in adult patients on high doses and/or long-term therapy of pyridoxine. We present the first case of pyridoxine toxicity in pediatric patient received therapeutic dose of pyridoxine of 1 mg/kg/day once daily who presented with low blood pressure, headache and hypersomnia.

4 Abbreviation: PN (pyridoxine), TB (Tuberculosis), PLP (pyridoxal 59-phosphate), RDA (Recommended Dietary Allowances), CKD (chronic kidney disease), ESRD (end stage renal disease), PDXK (pyridoxine kinase)

brain, PLP is required in the synthesis of different neurotransmitters important in both neuronal excitation and inhibition. It's then catabolized through the oxidation of pyridoxal to 4-pyridoxic acid, which is excreted in urine [21].

Daily recommended dose of vitamin B 6 varies according to the age of patient and indication of usage and form of supplementation. In pediatric age group, the daily-recommended dose increases with age. In our patient, 0.6 mg/day is the RDA of vitamin B6 with an upper limit of 40 mg/day of pyridoxine [21].We followed national guidelines and started the patient on 20 mg OD dose of pyridoxine for patient on isoniazid to prevent neurotoxicity.

Pediatric patients with chronic kidney disease (CKD) are at increased risk of complications especially those with advanced disease or on renal replacement therapy. As a result of reduce dietary intake, altered metabolism as well as dialysate-driven losses of watersoluble vitamins and select trace elements [7,10,13]. Add to that, these patients are on multiple medication that can alter the absorption and utilization of these elements.

Vitamin B6 deficiency has been observed in hemodialysis patients and well-studied. High-efficiency hemodialysis is leading to an even higher clearance of pyridoxine which sometimes found low even with replacement [14].

Unlike hemodialysis, children on peritoneal dialysis have either normal or high level of vitamin B6 without supplementation [15].

In recent meta-analysis, pyridoxine clearance is much lower in peritoneal dialysis than in hemodialysis, where mean serum levels can fall by 28-48 % depending on the dialyzer used [3, 7,11,18].

In animal study it was found that the susceptibility to pyridoxine-induced neuronopathy increases 5-to 10-fold in rats with renal failure upon chronic exposure. Furthermore, less than one week of protein deficient diet was able to accelerate and intensify the histological lesions and clinical signs of toxicity in these rats [17].

The clinical picture of PN induced neuropathy comes to our knowledge from clinical reports, patient typically present with sensory peripheral axonopathy involving stocking gloves distribution, however few cases report describes central and transit autonomic nerves system involvement **??**1]. Patient may suffer from paresthesia, hyperesthesia, bone pains, muscle weakness, numbness and fasciculations [2, 8,20] Although it may seem simple, identifying PN poisoning is quite challenging. When it comes to measuring plasma level of B-6 vitamer: Elevated PN plasma level is often not indicative of PN accumulation [22]. On the other hand, electrophysiological studies may aid in the diagnosis of sensory axonopathy, but it lacks any distinct characteristics [5]. Hence, clinician need to use their clinical judgment to safely reach to the diagnosis.

There is no reported treatment option. In majority of case reports drug cessation is needed. If the injury to the nerve is not advance, ganglions can regenerate leading to clinical improvement.

5 III.

6 Conclusion

Still there is little known to the pathophysiology of PN induced neuropathy. Therefore, we can conclude that in certain circumstances usage of pyridoxine supplementation should be used with cautions as in our patient. Parents should be counsel about the possible symptomatology that can develop overtime to their children. Vitamin B6 and CKD relationship is a complex that is not fully understood. Many reports suggest presence of an evidence of vitamin B6 deficiency in advanced CKD patient. Nevertheless, the intake and/or requirements of vitamins and trace elements in pediatric chronic kidney disease (CKD) or ESRD populations have not yet been studied in randomized controlled trials [12].

7 References Références Referencias

The exact mechanism of pyridoxine induced neuropathy (PN) is not well established. Proposed hypotheses include formation of reactive quinone methide, aldehyde toxicity through elevated PL/PLP concentrations, inhibition of PLP-dependent enzymes, andpyridoxal kinase (PDXK) inhibition [16,22,23]. Histopathologicaly it was found that toxic exposure to PN induced cell body degeneration of primary sensory ganglion and demyelination, consequently axonal degeneration. If exposed for long time, cell injury may result in irreversible damage [19]. [1]

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