Pregabalin Abuse During Pregnancy and Global Developmental Delay in Infants

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Abstract

Pregabalin is a medication licensed for the treatment of epilepsy and anxiety disorders. In addition, Pregabalin is increasingly recognised as a drug of abuse. Teratogenic effects have been demonstrated in animal models, however, there is a dearth of research relating to potential teratogenic effects in humans. This case highlights the potential role of intrauterine exposure to Pregabalin in contributing to Global Developmental Delay in two children.

Introduction:

Pregabalin is a medication which is classified as a gamma-aminobutyric acid, GABA analogue. In animal models, it has been demonstrated that in the central nervous system it reduces the release of excitatory neurotransmitters, which are probably associated with analgesic and anticonvulsant effects [1].

The United States Food and Drug Administration (FDA) approved Pregabalin for the treatment of neuropathic pain associated with diabetic peripheral neuropathy, spinal cord injury, postherpetic neuralgia and fibromyalgia, and as an adjunctive therapy for partial onset seizures [2]. However, over the last few years there has been increased abuse[3]. The frequent desirable effects reported by people who misuse Pregabalin include euphoria, relaxation, and sleep aid [4].We are presenting an interesting case of Pregabalin abuse in pregnancy and its likely impact on the child's development.

Case Presentation

Our case is a 29-year female referred by the general practitioner (GP) for inpatient Pregabalin detoxification. She was 16 weeks pregnant at the time of her admission. She reported that her GP initially prescribed her Pregabalin for anxiety in her early twenties and she could not discontinue due to withdrawal symptoms, she was taking 1400 mg of it daily.

She reported using Pregabalin in her last two pregnancies and developmental delay was diagnosed in both children. Child A, who is two and a half years old now, was born at full-term by normal vaginal delivery following an uncomplicated pregnancy. He was late to achieve his developmental milestones. He was diagnosed with global developmental delay by a multidisciplinary team and referred to the Early Intervention Team (EIT) at the age of 18 months.

Child B is 15 months old at the time of writing; she was also born at full-term via normal vaginal delivery following an uncomplicated pregnancy. All of child B's milestones were delayed and she was small for her age. She was diagnosed with Global Developmental Delay at one year of age.

Child A made significant improvements with intervention from the EIT and eventually reached his developmental milestones. Child B has not made much progress. There was no significant history of congenital abnormalities, learning disability or developmental delay in the parents or family of either child.

The mother was concerned about the impact of Pregabalin on the current pregnancy as she had been using higher dose of Pregabalin (1400mg) than in the previous pregnancies. She completed a four-week detoxification program and was referred to primary care.

Discussion

Global developmental delay can be defined as significant delay in two or more developmental domains: gross and fine motor; speech and language; cognition; personal and social development; or activities of daily living. “Significant” may be defined as performance at two or more standard deviations below the mean on developmental screening or assessment tests [5]. The diagnosis requires full clinical history, physical examination, routine baseline blood tests and specific blood tests e.g. creatinine kinase test, calcium assay, DNA studies and imaging CT, MRI and EEG [5].

We understand that currently there are few studies which examine the effects of pregabalin on pregnancy outcomes. Furthermore, there are even fewer studies which examine the immediate- and medium-term effects of pregabalin on the developmental milestones of children with a history of intrauterine exposure to high-dose pregabalin. One study which looked at the effect on pregnancy outcomes compared pregnancy outcomes in women exposed to pregabalin with those of matched controls (not exposed to any medications known to be teratogenic or to any antiepileptic drugs) [6]. A significantly higher rate of major birth defect and lower number of live births was observed in the pregabalin group, after exclusion of chromosomal aberration syndromes.

An Italian study identified 30 pregnancies that had been exposed to pregabalin and relative to unexposed pregnancies, exposure to pregabalin was associated with increased odds of many adverse outcomes; however, none of these were statistically significant [7].

According to our knowledge this is the first case report of the effect of pregabalin on developmental delay and there is little knowledge about the impact of pregabalin on the developmental milestones of children who were exposed to pregabalin during pregnancy. We hypothesize there may be different factors at play e.g., limited clinical trials studying the effect, more focus on other causes of developmental delay, reporting issues and pregabalin being a relatively newer drug.

Conclusions

This case explores the possible aetiological role of pregabalin in developmental delay in children exposed to it during intrauterine life but more research in this field is required to conclude this.

Declarations

i. Funding. The authors declared that this research received no specific grant from any funding agency, commercial or not-for-profit sectors.

ii. Conflicts of interest/Competing interests. The authors declared there is no conflict of interest with this research article.

iii. Ethics approval. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committee on human experimentation with the Helsinki Declaration of 1975, as revised in 2008. The authors assert that ethical approval for publication of this case report was not required by their local Ethics Committee. A written informed consent was obtained from the patient for preparation, publication, and presentation of this case report.

iv. Authors' contribution. All authors contributed to the case report. Initial case was identified by JK, initial template was also made by JK, formatting and final submission was done by JK. AC wrote abstract and proofread the completed manuscript. EF completed case report and a full proofread of manuscript. FF proofread the manuscript and provided advice about formatting.

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