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Use of Gabapentin as an Adjunct Agent in the Treatment of Neonatal Abstinence Syndrome: A Case Report

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Authors' contributions

This work was carried out in collaboration between both authors. Authors AB and MG wrote the draft of the manuscript and contributed to the correction of the draft. Author AB managed the literature searches. Author MG designed the figures. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

We report the use of Gabapentin (Neurontin), an anticonvulsant and analgesic, as a non-opioid adjunct agent in the treatment of a term newborn infant with neonatal abstinence syndrome (NAS). Initial treatment with methadone to prevent withdrawal symptoms was not fully effective. Despite the addition of clonidine, an alpha-2 agonist, he was still unable to be weaned off opioids. The addition of gabapentin reduced symptoms, allowing for successful taper off methadone, and discharge from the hospital. As a non-opioid agent, gabapentin is a drug with potential for assisting with the difficult task of treating NAS refractory to standard opioid therapy due to its sedative and analgesic properties without any respiratory depression.

Keywords: Neurontin; gabapentin; opioids; withdrawal; neonatal abstinence syndrome; clonidine; pain.

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1. INTRODUCTION

Neonatal abstinence syndrome (NAS) can occur after delivery in newborn babies who are exposed to opioids and other substances in-utero. Maternal use of opioid medications, such as methadone for the treatment of chronic pain syndromes or as replacement therapy for heroin use, exposes the fetus to these medications and increases the likelihood of NAS. A standard treatment plan consists of stabilizing the neonate on a dose of a long acting narcotic such as methadone, followed by slow reduction of this medication until the infant is weaned off the narcotic [1-4]. Adjuvant medications, such as the alpha-2 agonist clonidine and the barbiturate phenobarbital, as well as non-pharmacologic interventions, can be added to the methadone to aid in controlling symptoms and to wean the neonate off of narcotics. Despite these standard therapies some neonates will have symptoms that are difficult to treat. Gabapentin is a gamma-aminobutyric acid (GABA)-mimetic compound that is used as an anti-epileptic medication, as well as, in the treatment of chronic pain [5-7] and nociceptive pain [8]. In adult patients, Gabapentin has been used in acute post-operative pain management [9-11] and in opioid withdrawal [12-13]. We present the case of a newborn baby with NAS, in whom we used Gabapentin successfully to facilitate weaning off of opioids.

2. PRESENTATION OF CASE

A 3.5-kg male infant was born to a 30-year-old female who was taking methadone, 125mg per day, since conception. The mother continued the methadone throughout pregnancy as prescribed by her physician, for opioid dependency. She denied use of other substances and her toxicology screen was positive only for opioids. The baby was born by normal spontaneous vaginal delivery and was showing symptoms of NAS by 2 hours of age. The neonate experienced typical symptoms of NAS including tremor, high-pitched cry, increased tone, excessive sucking and regurgitation of formula. Other than the symptoms of NAS, physical examination and initial laboratory tests (complete blood count and basic metabolic panel) were within normal limits. Finnegan Abstinence scores were recorded as high as 18. Treatment is typically initiated for a Finnegan Abstinence score greater than 8. He was promptly treated with oral methadone 0.1mg/kg/dose given every eight hours. This dose of methadone partially controlled his symptoms but full control of the newborn's symptoms required a dose of 0.25 mg/kg/dose every 8hrs. After stabilizing at this dose for three days his methadone dose was decreased and a taper begun. The medical team attempted to decrease his dose every 2-3 days, approximately 5% per step. Typically infant's opioid doses are decreased if the Finnegan abstinence score is less than 5, and there is no scoring for insomnia. Scores over 8 will qualify the baby for rescue therapy. After only 2 steps of the taper, he was extremely irritable requiring several rescue doses of oral morphine 0.4mg/kg/dose. While this helped alleviate acute symptoms, his dose was unable to be decreased further. After two weeks, oral clonidine 10 mcg/kg/day divided every 8 hours was added, and given on alternating schedule to the methadone. Despite the addition of clonidine, and an increase in its dosage to 15 mg/kg/day, the baby's methadone could only be weaned to 0.15 mg/kg every 8 hours due to extreme irritability and poor sleep. The nursing staff had isolated the baby to decrease noise and was using several comfort measures including a rocking bed, soft music and frequent prone positioning. Despite all of the above the baby could not be weaned further. After consideration of all possible options, including adding phenobarbital or chloral hydrate, gabapentin was added as a third drug due to its properties of decreasing neuropathic pain with minimal respiratory depressive effects. The initial dose was 10 mg/kg/day given orally every eight hours (Fig. 1). It was gradually increased to a maximum of 20mg/kg/day, over the next week. After 48hrs the baby was remarkably less irritable and abstinence scores fell below 3. The taper was restarted and he was successfully weaned off methadone over the next 4 weeks. Once off the methadone, he was next tapered off clonidine over the next month as an outpatient, returning to clinic for monitoring. Finally, he was then weaned off the gabapentin over the next 2 weeks without any symptoms. The baby had no abnormal neurologic signs and was thriving at the last visit in pain clinic.

3. DISCUSSION

Fetal exposure to alcohol, tobacco, and drugs, including opioids, commonly occurs in the United States. The long acting narcotic, methadone, is frequently used in pregnant women for the treatment of chronic pain or as maintenance therapy in individuals previously addicted to heroin or oxycodone, leading to fetal exposure.

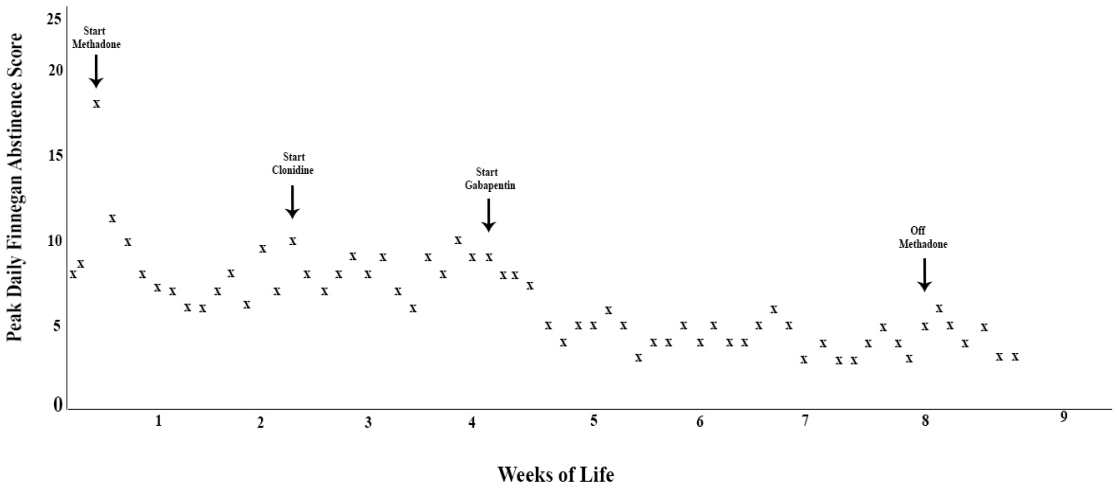

Fig. 1. Highest daily Finnegan scores with corresponding treatments

The majority of neonates [14] chronically exposed to methadone in utero will develop symptoms of neonatal abstinence syndrome, including tremor, high-pitched cry, increased tone, excessive sucking and regurgitation of formula. Treatment of NAS in these neonates includes both pharmacologic and non-pharmacologic therapies, with long-acting opioids, barbiturates and alpha-2 agonists as the mainstay of treatment. Despite these standard pharmacologic therapies some neonates have difficult to control symptoms of NAS. In these cases, non-pharmacologic therapies, such as removing the neonate from a stimulating environment, can be helpful. Rarely, these non-pharmacologic therapies are adequate by themselves and additional pharmacologic therapy is often necessary. Yet, in thoroughly reviewing the pediatric literatureusing PubMed, with key words neonatal abstinence syndrome, drug treatment, opioids, evidence of other drug treatment modalities remains scant.

Gabapentin is a GABA-mimetic medication originally used to treat spasticity and seizures. The use of Gabapentin has expanded to include treatment for nociceptive pain, such as peripheral neuropathy and diabetic neuropathy, as well as in chronic pain states such as trigeminal neuralgia, chronic headaches, and complex regional pain syndrome in adult and pediatric patients [15]. Its use in neonates has been described for pain management in neurologically impaired infants and in treatment of complex pain syndromes [16-18]. In animal studies Gabapentin restores the effects of morphine in rats chronically exposed to morphine [19]. In adult patients, Gabapentin may reduce the pain scores and total narcotic needs in opioid naïve patients in the acute postoperative period when continued through the perioperative course [9-11]. Gabapentin binds to the voltage-gated calcium channel, regulating the calcium channel and modulating the release of several neurotransmitters. It is unclear the exact mechanism by which Gabapentin reduces pain, but in adult patients there may be a reduction in opioid withdrawal when Gabapentin is used. It is easily absorbed when administered orally and is excreted in its original form by the kidneys. Our decision to use gabapentin was driven by a need for an adjunct to help taper infants who are clearly suffering withdrawal symptom during a taper. In the past we have used phenobarbital but noted in therapeutic doses, levels are often high, (greater than 20) causing moderate drowsiness and the potential for respiratory depression. The main advantage of Gabapentin is that there is not any respiratory depression, despite this medication providing some sedation and analgesia. In this and other cases since this patient, in our experience, unlike barbiturates, Gabapentin decreases NAS but the infants are much more alert and interactive. Thus, gabapentin is an ideal medication as an adjuvant when weaning in neonates with NAS. In pharmacokinetic studies, children less than 5 years of age had a reduced plasma concentration for a starting dose of 10/mg/kg/day as well as an increased clearance of the medication [20,21]. Given that most treatment protocols for seizures recommend starting at a dose of 10 mg/kg/day and increasing the dose every 1-3 days, this baby was started at this

initial dose. It was expected that the neonate would need larger doses and the dose was increased every 2 days until the symptoms were controlled and the abstinence scores decreased with a dose of 20 mg/kg/day divided into three doses daily. Once the NAS symptoms were stabilized, the opioid was then first tapered, followed by the clonidine and, finally, the gabapentin without any further difficulty. As nearly all medications used in neonates, including methadone and clonidine, which are now standard therapy for NAS, are also used 'off label', using Gabapentin in this patient was justified. Its use in infants and children as an anticonvulsant and analgesic and our experience in older children were the impetus for a trial of Gabapentin in this setting. Use of gabapentin was discussed with the family prior to starting therapy.

4. CONCLUSION

In summary, we report the use of Gabapentin in a neonate with difficult to control symptoms of NAS. The success in this neonate has led to the use of this medication in other infants who have failed conventional weaning methods and improved our ability to treat this disease. Further study, including a randomized, blinded trial, seems warranted.

CONSENT

All authors declare that 'written informed consent was obtained from the mother for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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