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Use of Donnatal™ Elixir in the Treatment of Neonatal Abstinence Syndrome

Alyssa Brzenski[1] and Mark Greenberg[1*]

[1]Department of Anesthesiology, University of California, San Diego, 200 West Arbor Drive, San Diego, CA 92103-8770, USA.

Authors' contributions

Both authors have read and approve of the manuscript. Both authors contributed equally to the creation and submission of this manuscript.

Case Study

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ABSTRACT

We present the case of a 6-week-old male infant with Neonatal Abstinence Syndrome (NAS) in which Donnatal™ (phenobarbital, hyoscyamine, atropine, hyoscine) Elixir was used as an adjunct therapy. The infant was born to a mother taking 130mg of methadone per day since conception. Due to NAS, he was treated with a methadone taper and oral clonidine. Yet, despite the majority of symptoms being suppressed with these medications, he remained stricken with colicky pain, unresponsive to supplemental opioids. A trial of Donnatal™ resulted in relief of symptoms and completion of his opioid taper. We recommend Donnatal™ as part of the treatment plan for refractory abdominal symptoms in cases of NAS.

Keywords: Donnatal™; belladonna alkaloids; withdrawal; colic; neonatal abstinence syndrome; visceral abdominal pain.

1. INTRODUCTION

Neonatal Abstinence Syndrome (NAS) can occur after delivery in newborn babies who are exposed to opioids and other substances in-utero. Various treatments are available for opioid tolerant infants, including the use of an opioid, in combination with adjuvant medications such as the alpha-2 agonist clonidine and the barbiturate phenobarbital. A

**Corresponding author: Email: mgreenberg@ucsd.edu;*

standard treatment plan consists of stabilizing the infant with an opioid such as morphine or methadone, followed by a slow taper of the opioid dose over the next few weeks until the infant is weaned off opioids [1-4]. Gastrointestinal symptoms, including hyperphagia, vomiting and loose stools are symptoms of NAS and are controlled once an adequate dose of opioid is administered [5]. Yet, many infants develop colicky visceral abdominal discomfort during the taper of the opioid, prolonging the duration of the taper. Caretakers note that the baby will be 'gassy' and cry intermittently, unrelated to the timing of feedings. Simethicone [6] and oral sucrose [7] have been tried with minimal effect. Donnatal, a mixture of the Belladonna alkaloids hyoscyamine, atropine, and hyoscine, combined with the barbiturate phenobarbital, has been used for intestinal hypermobility syndromes including infantile colic [8], irritable bowl syndrome [9] and duodenal ulcers [10]. We present the case of a newborn baby with NAS, in whom we used Donnatal successfully to facilitate weaning off opioids.

2. PRESENTATION OF CASE

A 3650-gram male infant was born to a 32-year-old female who was taking 130mg of methadone a day for the treatment of opioid dependence. The mother, who had used oxycodone in the past, was taking methadone since conception and continued the medication throughout the pregnancy. She denied using tobacco at anytime during her pregnancy. The baby was born at term, via an uncomplicated vaginal delivery, and was cared for in the Neonatal Intensive Care Nursery, due to the likelihood of developing opioid withdrawal. Maternal and neonatal drug screens were only positive for opioids. After 12 hours the baby exhibited sweating, high-pitched cry, loose stools, hyperphagia and insomnia. His Finnegan NAS score was 14 and he was immediately started on oral methadone 0.1mg/kg/dose given every 8 hours. The baby also had a 0.1mg/kg orders for oral morphine solution for breakthrough symptoms, where the abstinence scores were greater than 8. The baby continued to have symptoms and over the next 72 hours the methadone dose was increased to control symptoms, finally stabilizing the baby at 0.25mg/kg/dose every 8 hours. Once the baby was symptom free and feeding normally the methadone was gradually tapered every 3-5 days as tolerated. After 2 weeks, oral Clonidine suspension 10mcg/kg/day divided every 8 hours was added to aid in weaning off the opioids (Fig. 1). The methadone and the clonidine were alternated so the baby was getting a medication every 4 hours.The mother abstained from breastfeeding after delivery.

After 6 weeks the baby was having difficulty weaning his methadone any further. His methadone dose at that time was 0.08mg/kg/dose. Any attempts at a further reduction in dose resulted in significantly higher NAS scores and need for rescue doses of morphine. Examination of the infant revealed a mildly distended abdomen at times, and his symptoms seemed to be relieved by the passage of gas. A trial of simethicone was ineffective and an abdominal radiograph was normal. He had normal appearing, heme negative stools. A trial of Donnatal, 0.1ml/kg given every 6 hours PRN perceived abdominal pain, was started. The baby received 3 doses on the first day, and 2 doses on the second and third days thereafter. On the 4th day after starting the Donnatal, the methadone taper was resumed. He continued to receive Donnatal, but only once a day on average. He was successfully weaned off methadone over the next 3 weeks, without interruption. He was discharged and the clonidine was tapered over the next month at home. On follow up in pain clinic the baby was asymptomatic and growing normally.

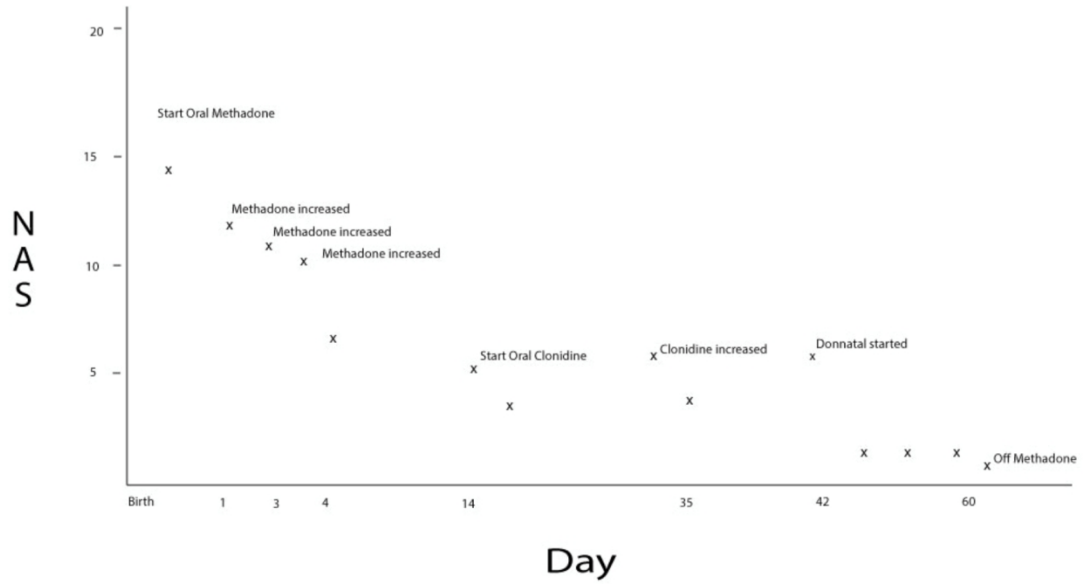

Fig. 1. Plot of NAS finnegan scores during the days after birth. Clinical course is noted next to plotted scoring

3. DISCUSSION

Fetal exposure to alcohol, tobacco and drugs, including opioids, commonly occurs in the United States. Chronic methadone therapy in pregnant women is used for treatment of chronic pain or as maintenance therapy in individuals previously addicted to heroin or oxycodone, leading to fetal exposure. NAS from opioid withdrawal occurs in up to 80% [11] of neonates chronically exposed to methadone in-utero. Treatment of NAS in these neonates includes both pharmacologic and non-pharmacologic therapies, with opioids, barbiturates and alpha 2 agonists used as the mainstays of pharmacologic therapy. Clinical factors, including maternal smoking, psychiatric medications and lack of breastfeeding can increase the incidence and severity of NAS [12-14]. In addition, early data suggests that genetic factors, such as single polymorphisms in μ-opioid receptor and catechol-o-methyltransferase genes, may decrease the severity of NAS [15]. However, in some infants these medications may be ineffective in treating the visceral abdominal pain associated with opioid withdrawal. Diarrhea, vomiting and hyperphagia are known components of opioid withdrawal and usually respond well to opioid replacement therapy. As the tapering of opioids progress in the course of treating NAS, we have noticed that the babies develop signs of colicky visceral discomfort. Simethicone, an anti-foaming agent has been used for the treatment of gas pains and infantile colic, but the results are disappointing in both colic and in infants undergoing opioid weaning. In lieu of other effective treatments, we have used simethicone in the past, but its efficacy has been unimpressive.

In this case, Donnatal Elixir was chosen to treat the abdominal discomfort that the infant exhibited because the combination of compounds in Donnatal provides a rational therapeutic mixture of agents to treat visceral abdominal pain associated with NAS. Donnatal, a mixture of belladonna alkaloids and phenobarbital has the following composition:

Each 5mL Donnatal Elixir contains:

Phenobarbital	15mg
Hyoscyamine Sulfate	0.1mg
Atropine Sulfate	0.02mg
Hyoscine Hydrobromide	0.007mg
Alcohol 100%	24% vol/vol

The anticholinergic properties in the belladonna alkaloids are potent antispasmodics, and likely help decrease perceived abdominal gas pains. Phenobarbital produces mild sedation, decreasing the anxiety component of the pain, thereby helping calm the infant. Yet, at the dose administered it is unlikely that significant sedation is produced. The phenobarbital dose in this patient (using 0.1ml/kg) was about 1.5mg/dose, which if given on average of once per day, is about 0.3mg/kg/day. The one level we did get after 2 weeks was only 1.4mg/dl, making it unlikely that the phenobarbital was having the sole therapeutic effect. Since the mixture is dissolved in ethyl alcohol, a central nervous system and smooth muscle relaxant, it is possible that the ethanol is contributing to the symptomatic relief. Given the complex nature of infantile colic, it is most likely the combination of all of the agents in the mixture were contributing to the decrease in the infant's symptoms. Following the successful treatment of this infant's abdominal pain, we have made PRN use of Donnatal, in infants with protracted NAS, a routine since this case with a very significant decrease in NAS treatment failures.

4. CONCLUSION

In summary, we report the use of Donnatal, a mixture of phenobarbital and Belladonna alkaloids, for the visceral abdominal discomfort we perceive that the infants with NAS are experiencing. The success in this case has led to use in other infants, and improved our ability to treat this disease.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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