

Pregabalin, A Neuropathic Drug Used as an Antitussive In A Pediatric Child With Acute Cough

A Case Report

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Abstract

Cough is a very common symptom causing medical consult. Several remedies are readily available in the market however these are currently not recommended among the pediatric population due to a few reasons which include the benign nature of acute cough, limited effectivity and lack of support from the United States Food and Drug Administration (USFDA) due to abuse potential.

We report a case of a 2-year-old male, no known co-morbidities with a 2 week history of upper respiratory tract infection. Initial assessment showed viral infection hence patient was given medications for symptomatic treatment. However, 1 week after, patient still presented with symptomatic persistent coughing that disrupted his activities of daily living, hence antitussive medication was already prescribed. After another 7 days, there was still persistence of symptoms, hence patient was given a trial medication of Pregabalin 0.7 milligram/kg/dose which noted instant cough relief one hour after the initial intake. Patient also reported to be more playful, improved sleep at night and improved appetite. Patient received total of 2 doses of Pregabalin in the span of 48 hours. On the third day, patient was still coughing but reported to be significantly less frequent and more productive, hence medication was then put on hold. Patient continuously improved after 5 more days and was eventually cough free.

This case report demonstrates the adequacy of Pregabalin as a supportive antitussive medication in a patient with an acute cough secondary to a viral infection

INTRODUCTION

Cough is one of the most common symptoms in children. Acute cough in the pediatric population is one the most common cause of caregivers seeking medical consult.¹ Unlike in the adult population, the definition of acute cough in the pediatric community is not well established and it varies according to different sources. According to Vogelberg, C et al, (2023), acute pediatric cough lasts from 4-8 weeks, however, other experts defined it as cough lasting from 2-8 weeks.²

Acute cough is mostly caused by a benign upper respiratory tract infection. Although there may be numerous different possible etiologies, viral source is still the most common. Infection or foreign particles in the airway causes bronchospasm causing continuous coughing. Acute cough is also believed to function as a protective reflex to help clear excessive secretions in the respiratory tract.^{2,3}

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Acute pediatric cough with viral etiology would usually resolve on its own without treatment. Even so, there have been significant number of medications that has been formulated for cough suppression that has been sold readily in the market. Among which include Dextromethorphan, Antihistamines, Vapor Rubs, Honey, Codeine, Promethazine, Benzonatate and Inhaled Corticosteroids.¹

Among the available cough medications, a lot has not been proven to be very much effective and many are still not regulated by the United States Food and Drug Administration (FDA). On top of this, acute cough has been regarded to be benign and self-limiting for majority of the upper respiratory tract infections. These reasons have caused a lot of pediatricians to shy away from prescribing antitussives to this certain diagnosis and its use has not been recommended by the pediatric treatment guidelines. However, persistent cough can significantly affect both the lives of families and children as it can greatly influence the child's quality of life.^{1,3} Continuous coughing among children is a great source of stress among caregivers most especially if the child refuses to eat, gets an undisturbed sleep and decreased level of activity.²

Antitussives although not routinely recommended to very young children can be considered if there is parental concerns or the medication is proven to be effective with little side effect^{1,3}

OBJECTIVES

1. To present a Pediatric Case of cough neuropathy.
2. To present the use of low dose Pregabalin in the symptomatic treatment of a Child with Neuropathic Cough

SIGNIFICANCE

Acute cough in the pediatric population has not

received the same treatment strategies unlike the adult population. The lack of effectivity of most available drugs and the fear of exposing a vulnerable population to new treatments makes it hard to look and try for new possible more effective medication. This case report presents the use of Pregabalin in the management of acute neuropathic type of cough.

CASE HISTORY

This is a case of a 2-year-old male patient who had 2 weeks history of persistent dry neurogenic cough. The case informant is the child's mother with 80% reliability. The patient lives with his parents and a sibling in a 2-story home with exposure to secondhand smoke. Patient had an unremarkable prenatal, birth and post-natal history. There was no history of hospitalizations, allergies, or comorbidities and is also known to have complete vaccination for age.

3 days prior to consult, our patient presented with high-grade fever (39-40 degrees Celsius) associated with coryza, conjunctivitis and non-productive cough. This was initially not associated with vomiting, diarrhea, rashes or change in appetite. There was a history of exposure to sick relatives who presented similarly. This prompted consult and remarkable physical examination showed purulent bilateral eye discharges and rhinorrhea. Patient was given Paracetamol at 15 milligram/kg/dose every 4 hours alternating with ibuprofen at 10 milligram/kg/dose every 6 hours as needed for fever, Cetirizine 2.5 milligram

2 times a day, Montelukast 4 milligram once a day and Salbutamol nebulization 1.25mg + normal saline solution 3x a day. Sodium Chloride nasal spray with nasal suctioning was also done as needed.

Interim there was resolution of fever, conjunctivitis and coryza however there was note of persistence of dry cough, neurogenic in

character. Hence 4 days after, follow-up was done where patient was given additional medications which include: Levodropropizine syrup at a dose of 1milligram/kg 3x a day, Manuka Honey 5mL once a day and chest physiotherapy.

7 days after, patient was then brought back for consultation due to persistence of cough. Mother reported that the coughs frequency is every 30 seconds while patient was able to report his throat to be very itchy causing persistent coughing. He was unable to eat and sleep due to the persistent cough with occasional post-tussive vomiting. On further examination, patient was awake, alert but did not want to leave his mother. He lost 2 pounds from baseline weight. There were no retractions, clear breath sounds, normal heart rate and rhythm for age, abdomen soft and non-tender, full pulses, and decreased skin turgor. Mother was offered to be admitted, however refused.

Patient was then given Pregabalin 0.7 milligram/kg and was then advised to wait for observation. One hour after the intake, there was note of resolution of cough. The patient was then able to take his regular meal then went to afternoon nap lasting for 2 hours. Upon waking up, patient was up and about, still with minimal occasional coughing episodes but was able to tolerate take his regular meals. Patient was sent home and was advised to make a diary on patients' behavior, sleep, cough and feeding pattern.

Patient was reported to have uninterrupted sleep with no coughing episodes at night, good appetite, and playful behavior. 20 hours from the initial intake of Pregabalin, there was note of recurrence of persistent coughing episodes with associated poor appetite and post-tussive vomiting. Another dose of Pregabalin of 0.7milligram/kg was given which was seen to take effect after one hour. The medication was subsequently given as needed (20-24 hours interval) for the persistent coughing but not more than two times a day.

The patient continuously improved after 3 days from the initiation of medication, still with coughing episodes but significantly less frequent. He had good appetite, was playful and good sleeping pattern, hence medication was discontinued.

11/10/2023		
Medications: Cetirizine, Salbutamol Nebulization, Montelukast, Nasal Suctioning		
Cough	Bad	Dry cough every 30 seconds
	Good	
Sleep	Bad	Poor sleep due to cough
	Good	
Appetite	Bad	Poor appetite, unable to take favorite food
	Good	
Activity	Bad	Refused to play.
	Good	
11/11/2023		
Medications: Cetirizine, Salbutamol Nebulization, Montelukast, Nasal Suctioning, Pregabalin		
0.7mg/kg/dose (1 dose only at 1pm in the afternoon)		
Cough	Bad	
	Good	Approximately 1 hour after pregabalin, the coughing stopped
Sleep	Bad	
	Good	Slept 3-5:30 pm (regular nap time) and was able to sleep overnight uninterrupted with coughing episodes.
Appetite	Bad	
	Good	Fair appetite and was able to request fried chicken for dinner.
Activity	Bad	
	Good	Was able to separate from his mother and watch his favorite television show, afterwards he was able to play with his sister.
11/12/2023		
Medications: Cetirizine, Salbutamol Nebulization, Montelukast, Nasal Suctioning; Pregabalin		
0.7mg/kg/dose (2nd dose given at 9 AM in the morning)		
Cough	Bad	Before the intake of second dose of pregabalin, recurrence of frequent coughing
	Good	Resolution of cough 1 hour after intake of Pregabalin
Sleep	Bad	
	Good	Was able to sleep the night before but woke up with recurrence of coughing
Appetite	Bad	
	Good	Improving appetite as compared to 11/11/23
Activity	Bad	
	Good	Playful
11/10/2023		
Medications: Cetirizine, Salbutamol Nebulization, Montelukast, Nasal Suctioning, Pregabalin put on hold		
Cough	Bad	
	Good	With intermittent productive cough
Sleep	Bad	
	Good	Good sleep
Appetite	Bad	
	Good	Good appetite
Activity	Bad	
	Good	Playful

Table 1: Diary created by patient's caregiver

DISCUSSION

We presented a case of a 2-year-old male with acute cough initially coming from a viral illness. Patient was initially treated symptomatically including cough suppressants however, there was note on persistence of symptoms causing the child to have poor quality of life.

Acute viral cough is known to be self-limiting. It can present to be dry or productive in character. For the pediatric population, symptomatic treatment is usually not recommended because these treatments are known to be not more than effective than placebo. Primary medical approach in the treatment for viral infection is limited to hydration.

The American Academy of Pediatrics (AAP) recommend against the use of over-the-counter antitussive medications stating that it is no more effective than placebo for reducing cough from viral respiratory infection in children.⁴

The use of antitussives in the pediatric community have been in question for so many years now, however, the over-all adverse event rate has been very low. In the study of Lam, S et al, (2021), stated that in an extensive review done in a multisystem surveillance program, the adverse event rate of cough and colds medication in children younger than 12 years of age was 1 case per 1.75 million units sold. 0.6% (20/3251) resulted in death wherein none involved a therapeutic dose.

The self-limiting nature of acute cough in children have led many physicians not to make it a major symptom to be addressed. However, there are instances wherein cough becomes debilitating to very small children. Cough is not merely a respiratory symptom, it can also be controlled via the central mechanism known as: Reflex, voluntary and evoked type of cough. The initiation and inhibition of cough reflex is under the control of higher neurological centers. While there are many central nervous system conditions causing increased cough reflex sensitivity, a simple viral

infection can cause post viral vagal neuropathy. According to Mohammed A.B, et al. (2022), cough reflex hypersensitivity from vagal neuropathy can present as cough spells triggered by low threshold stimuli in a patient's regular daily activities (exposure to a changing temperature, aerosols, perfumes, odors, or during talking or laughing). It can either be acute or chronic but always manifests predominantly as cough.⁹

Pregabalin is a voltage gated calcium channel blocker that decreases synaptic release of several neurotransmitters. It was initially formulated as an antiepileptic drug however is now approved by the FDA to be primarily used as a treatment for neuropathic pain only in the year 2007. It has several off-label use and one of which is for chronic cough for adult patients^{5,6} Several studies have shown Pregabalin have been used as a possible treatment of chronic refractory cough.^{10,11} In the pediatric population, it has been studied as an adjunctive therapy for focal onset seizure. In a recent paper made by Chan, P. et al, (2021), they recommended that as an adjunctive antiepileptic medication, Pregabalin should be used with the following doses.

1. 3.5 milligram/kg/day (maximum of 150 milligram/day) divided as two to three doses for <30 kilograms
2. 2.5 milligram/kg/day (maximum of 150 milligram/day) divided as two to three doses for $\geq$ 30 kilograms.

There are no available data on the use of pregabalin as a cough suppressant in the pediatric population. The development of pediatric drug use, safety and dosing is generally difficult as the subjects involved are vulnerable, making it hard to collect subjects.

To the best of our knowledge, this is the first case report regarding the use of Pregabalin as a cough suppressant in a pediatric patient suffering a neurogenic type of cough.

RECOMMENDATIONS

The Model-Informed Drug Development is a powerful tool that was developed last 1990. According to Bi, Y. et al., (2021), the tool can integrate and leverage the existing knowledge from different sources to narrow gaps. It can hasten the development of new medication and has been shown to result in better estimation of medication dosing especially in the pediatric population.⁸ Our case report recommends the use of this tool for possibly the development and use of Pregabalin in the neurogenic type of cough in the pediatric population.

CONCLUSIONS

The introduction of new drugs to the pediatric population is difficult. Careful titration of medication to determine the effective and right dosing is important. Our study has demonstrated the effectiveness of using Pregabalin as a supportive antitussive drug in the treatment of a Filipino child with an acute cough.

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