CASE SERIES

Benzonatate Induced Neck Stiffness: A Case Series

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ABSTRACT

As a non-narcotic antitussive, benzonatate has been effective in symptomatic relief of dry cough. Cough following recovery from acute COVID-19 has widely been treated with over-the-counter cough suppressants like benzonatate, guaifenesin, dextromethorphan etc. However, despite being an effective non-narcotic cough suppressant modality, benzonatate has been constrained by its poor safety profile. The present case series describes a very rare side effect of neck stiffness reported in patients who were prescribed benzonatate for dry cough suppression post COVID 19.

KEY WORDS: Benzonatate, Neck stiffness, Post-COVID complications, Cough.

Introduction

Coronavirus disease (COVID-19) pandemic has affected mankind to its large extent with its clinical manifestations ranging from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome (ARDS), septic shock, and multi-organ failure resulting in death.[1]In about 60–70% of symptomatic COVID-19 patients, dry cough has been one of the most common initial symptoms of COVID-19, with its median time to onset being 1 day and mean persistence of 19 days.[2] An online survey noted that 20 — 30% post covid patients still reported experiencing dry cough after 2 to 3 months of the disease.[2,3]

Benzonatate, a non-narcotic oral antitussive drug has been significantly used to relieve and suppress cough in patients older than 10 years. The drug was approved by US-FDA in 1958 and is available in the United States as 100-mg and 200-mg yellow liquid-filled spherical capsules under the brand name Tessalon Perles.[4] In India, benzonate is available under the brand name of Benz. The drug has sodium channel-blocking properties and anesthetic effects on the stretch receptors in the lungs & suppressing the cough reflex in the brain.[5] Although benzonatate is a non-opioid and not prone to abuse, it has a poor safety profile. Common side effects associated with this drug include sleepiness, dizziness, headache, upset stomach, skin rash, hallucinations, allergic reactions. However, overdose of this medication has been reported to cause altered mental status, coma, seizures, hypotension, tachycardia, ventricular dysrhythmias, and cardiac arrest.[4,6] Management of benzonatate toxicity begins with supportive care and continuous monitoring of neurologic and cardiovascular status. Thus, use of this drug mandates caution. Onset of action is usually within 20 minutes, with its duration of action lasting upto 8 hours.[7] The drug has its structural resemblance with other local anesthetics, including tetracaine and procaine.

In this case series we describe a very rare side effect of neck stiffness reported in patients who were prescribed benzonatate for dry cough suppression post COVID 19 recoveries.

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Case 1

A 25-year-old female presented to the Medicine OPD with complaints of neck pain and stiffness for the past 24 hours. Patient was tested positive for SARS-CoV2 virus, 10 days back. On recovery, she was suffering from dry cough and visited a local

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physician two days back to her present-day visit, who prescribed Capsule Benzonatate 100mg thrice a day. Her cough significantly decreased within a day, but she developed excessive neck pain and stiffness. Benzonatate was discontinued and she was symptomatically treated with muscle relaxants, NSAIDs and a mild expectorant. Her neck stiffness subsided within the next 48 hours. No breathing difficulty or pain was noted on further follow up.

Case 2

A 32-year-old male with COVID-19 positivity tested one week earlier, presented to the facility with complaints of severe neck stiffness for the past 48 hours. During history taking, the patient revealed that he was suffering from a severe dry cough along with a headache for which he consulted a local physician who prescribed him Dextromethorphan lozenges. However, his cough was not relieved, following which the physician prescribed him Cap. Benzonatate 100mg four times a day. Within 36 hours of initiating benzonatate therapy, the patient experienced marked improvement in dry cough, but developed a stiff neck which was accompanied with gradually increasing pain. On reporting to the present facility, benzonatate was withdrawn, and he was treated with muscle relaxants and NSAIDs, along with hot water fomentation for relief of pain and stiffness. Patient gradually reported recovery from pain and stiffness within the following 36 hours. No further complaints were noted.

Case 3

A 38-year-old male with a history of COVID-19 positivity, tested 14 days back, presented with complaints of severe cervical pain and nausea. Patient gave a history of suffering from dry cough for 10 days for which he was prescribed a mild cough syrup containing ambroxol and salbutamol. However, his cough did not subside, and on revisit to the concerned physician, he was shifted to benzonatate therapy with Cap. Benzonatate 100mg thrice a day. Patient reported marked improvement of cough, but developed cervical pain, stiffness and nausea within 36 hours of initiation on Cap Benzonatate. On reporting to the present facility, benzonatate was suspected and withdrawn. Patient was treated with muscle relaxants, NSAIDs, hot water fomentation, which relieved his stiffness in the following two days. However, no further complaints were noted on follow up.

All three cases were assessed to be under the 'probable' category of causality scale as assessed by WHO-UMC Causality Assessment Scale.[8] Severity of the cases were moderate with level 3 on Hartwig-Siegel Scale.[9]

Discussion

Benzonatate, also known as 4-(butylamino) benzoic acid, bears structural resemblance to tetracaine and the ester-linked class of local anesthetics, which results in a similar mechanism of action and toxicity profile as local anesthetic agents. Benzonatae, after its oral ingestion and subsequent systemic absorption via the gastrointestinal tract, acts peripherally by directly anesthetizing the vagal stretch receptors in the respiratory passages, lungs, and pleura. Benzonatate has sodium channel blocking property which explains neurological and cardiovascular toxicity on overdosing. On a milder note, it might be this sodium channel blocking that causes depolarisation of the skeletal muscles and thus the stiffness. However, the plausible mechanism still remains unclear.

As a non-narcotic antitussive, benzonatate has been effective in symptomatic relief of dry cough. Cough following recovery from acute COVID-19 has widely been treated with over-the-counter cough suppressants like benzonatate, guaifenesin, dextromethorphan etc. However, despite being an effective non-narcotic cough suppressant modality, benzonatate has been constrained by its poor safety profile. Listed adverse reactions with this drug includes hypersensitivity reactions (bronchospasm, laryngospasm, cardiovascular collapse), mild CNS events (sedation; headache; dizziness; mental confusion; visual hallucinations), gastrointestinal events (constipation; nausea; GI upset), cutaneous manifestations (pruritus, skin eruptions) and others (nasal congestion; sensation of burning in the eyes; vague "chilly" sensation; numbness of the chest).[10] To our knowledge this is the first case vignette reporting neck stiffness secondary to benzonatate use as an unlisted adverse reaction to this drug. As reported in all three of our cases, 50-60% decrease in cough frequency was noted within 24-36 hours of drug intake. However, all three cases reported experiencing stiffness and pain in the neck developing within 24 to 48 hours of benzonatate intake, which also subsided on the drug discontinuation.

Conclusion

Benzonatate is a unique antitussive medication with sodium channel-blocking properties that may cause moderate to severe adverse effects respective to its daily dosing. Thus, rational prescribing with limited dosing and constant follow-up is warranted. Safety profile of a drug should also be explained to the patients in order to prevent adversities and ensure prompt identification, early treatment and recovery.

Source of Support

Nil

Conflict of Interest

None

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and/or clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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