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# Epileptic Seizure After Treatment with Thiocolchicoside: A Case Report

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## Abstract

**Background:** Adverse drug reactions are important determinants of inpatient and outpatient morbidity. Thiocolchicoside is a semisynthetic derivate of naturally occurring colchicoside, which is largely used in humans as a centrally acting muscle relaxant. Epileptic seizures after thiocolchicoside intake have been reported in individuals with a history of epilepsy, acute brain injury or possible blood–brain barrier disruption.

**Case report:** A 25-year-old Kashmiri girl presented to Emergency department of general medicine with history of generalized tonic clonic movement of all the four limbs associated with up rolling of eyes, urinary incontinence and frothing from mouth of 15minutes duration. She had developed first time GTCS in her life she was admitted for evaluation she remained in post ictal state for 2days and regained consciousness after 2days. She was seizure free for 6days in hospital.

**Discussion:** Drugs only rarely cause focal seizures. Our case indicates that thiocolchicoside can precipitate seizures in predisposed patients, and that its use should be avoided in patients with brain diseases (and therefore lower seizure thresholds) or blood–brain barrier disruption. This information should be provided in the drug package insert.

**Keywords:** adverse drug reaction, thiocolchicoside, coltrax, epileptic seizure, muscle relaxant

## Introduction

Adverse drug reactions are defined as noxious, unintended or undesired effects of any drug used for

prophylaxis, diagnosis or therapy. Such effects constitute an important determinant of inpatient and outpatient morbidity. According to the drug package insert, the main adverse effects of thiocolchicoside (Coltrax®; AventisPharma) are nausea, somnolence, asthenia, allergy and vasovagal reaction. It is contraindicated in patient with history of drug allergy or vasovagal reaction during previous utilization.

Thiocolchicoside is a semisynthetic derivate of naturally occurring colchicoside, which is largely used in humans as a centrally acting muscle relaxant. This compound also has anti-inflammatory and analgesic effects. It is an analogue of colchicine, since they share the same benzo (alpha)heptalenic moiety.

The experimental use of colchicine has been shown to induce epileptic foci in rats, causing generalized seizures and death. 3–5 The epileptogenic activity of thiocolchicoside occurs mainly when there are minimal lesions of the dura and arachnoid membranes.

Epileptic seizures in humans have also been reported in patients with a history of epilepsy, acute brain injury or possible blood–brain barrier disruption.

Here, we report a case of sudden epileptic seizure temporally related to intake of thiocolchicoside for cervical neck pain.

**Case Report**

A 25-year-old Kashmiri girl presented to Emergency department of general medicine with history of generalized tonic clonic movement of all the four limbs associated with up rolling of eyes, urinary incontinence and frothing from mouth of 15minutes duration. She had developed first time GTCS in her life she was admitted for evaluation she remained in post ictal state for 2 days and regained consciousness after 2days. She was seizure free for 6 days in hospital.

This occurred after intake of thiocolchicoside for 3 days (4 mg bid, in a total dose of 24 mg), as prescribed for neck pain. Seizures began 6 hours after the final dose. The results of the neurological examination were normal. The thiocolchicoside was discontinued, and IV levepil anticonvulsive therapy was initiated. These seizures were thus controlled, and there were no further episodes for the duration of 6 days in hospital.

An additional MRI scan was ordered. CEMRI brain was normal. Electroencephalography and angiography findings were normal. CSF analysis was normal. Autoimmune panel, viral panel for CSF was normal. ANA profile was also normal.

The results of thorough laboratory testing (cell counts; glucose level; erythrocyte sedimentation rate; serum levels of protein, Na, K, Ca, Mg, P, alanine aminotransferase, ALT, gamma-glutamyltranspeptidase, alkaline phosphatase and bilirubin; coagulation tests; creatine kinase level; urea nitrogen level; creatinine level; autoantibody titers; complement activation; and urine exam) were normal.

Levepil was continued and patient was discharged home on levepil 500mg BD for at least 6months. She was kept on OPD follow up after that.

**Discussion**

This is the fifth case reported in the literature in which a relationship between seizures and thiocolchicoside was demonstrated. 6 The three other cases occurred in Italy (our patient was of Italian descent), and this is the second case in which there was no history of seizures. In the two cases in which there was a history of epilepsy, the patients had been seizure-free for 7 and 9 years, respectively, and presented disease exacerbations only after thiocolchicoside intake. The other case in which there was no such history was in a 40-year-old male patient who had been in a traffic accident and presented

CT-proven cerebral contusion of the left hemisphere. Intramuscular thiocolchicoside was administered (4 mg bid). Approximately 30 minutes after the second daily injection, the patient had a generalized tonic–clonic seizure.

The mechanism of action of thiocolchicoside is only partially understood. Previous studies have suggested that it has an agonist interaction with spinal-strychnine-sensitive receptors that could mediate its myorelaxant effect, 8 although such interaction does not readily explain how it might induce seizures. 6 Another study demonstrated a pharmacological profile indicating a preferential interaction of this compound with a cortical subtype of the gamma-aminobutyric acid type A (GABAA) receptor that expresses low-affinity binding sites for GABA. The low-affinity recognition site seems to be an antagonist-binding site, a finding that can readily explain the powerful convulsant effect of thiocolchicoside observed in some humans. 6,9

The convulsant potential of thiocolchicoside is likely to involve an overwhelming effect of drug antagonism at a subset of GABAA receptors over the drug inhibitory effect of allosteric activation of strychnine-sensitive glycine receptors. 5 Another study provided molecular evidence that the epileptogenic activity of thiocolchicoside might be due to inhibition of the function of inhibitory receptors in the central nervous system. 10 Thiocolchicoside induced epileptic seizures and even death in rats that received this drug parentally, at the dosage of 6 to 12 mg/kg, although only in rats that had minimal lesions of the dura and arachnoid membranes. 5

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