CASE REPORT

Acute ischaemic colitis associated with oral phenylephrine decongestant use

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SUMMARY

In this case, the authors have presented for the first time that ischaemic colitis may be associated with phenylephrine use. Since phenylephrine is the more common active ingredient in over-the-counter (OTC) cold medications, other presentations may follow this case. A MEDLINE search was performed for all case reports or case series of ischaemic colitis secondary to pseudoephedrine or phenylephrine use published between 1966 and 2013. The search resulted in four case reports and one case series describing patients with acute onset ischaemic colitis with exposure to pseudoephedrine immediately prior to onset. However, we found no case reports of ischaemic colitis associated with phenylephrine use. We present this case as an unexpected clinical outcome of phenylephrine, which has not been associated with ischaemic colitis in the literature. Also, this case serves as a reminder of the important clinical lesson to question all patients' use of OTC and prescribed medications.

BACKGROUND

Ischaemic colitis is a well-defined disease process usually diagnosed by colonoscopy and biopsy. Ischaemic colitis usually presents in older adults as a complication of vascular disease with symptoms of acute abdominal pain followed by haematochezia. The differential for this type of presentation is broad and includes infectious aetiology, inflammatory bowel disease and malignancy.

Several case studies have suggested that pseudoephedrine use is a potential cause of ischaemic colitis.^{1–5} The drug pseudoephedrine is an indirect β -adrenergic and α -adrenergic receptor agonist, and is commonly used as a nasal decongestant because of its vasoconstrictive properties on the nasal mucosa.⁶ In addition to its effects on the nasal mucosa, it is believed to cause vasoconstriction in other parts of the body including the heart⁷ and the mucosa of the colon, thus leading to ischaemia.^{1–5}

In recent years, many pharmaceutical companies have transitioned away from using pseudoephedrine as an active ingredient in their cold and nasal decongestant over-the-counter medications because the Combat Methamphetamine Act (CMEA) of 2005 made its sale increasingly difficult. The new restrictions require sellers to store the products 'behind-the-counter' or in locked storage containers and regulate/record the amount of products sold to an individual.⁸ Therefore several companies changed the active ingredient in their decongestant medications from pseudoephedrine to phenylephrine, a vasoconstrictor with direct acting

α -1-agonist with weak α -2-agonist and β -agonist activity.^{6,9}

We present the first case report linking phenylephrine use with ischaemic colitis.

CASE PRESENTATION

A 70-year-old African-American woman with a medical history significant for hypertension, hyperlipidaemia and diverticulosis presented to the emergency department (ED) with acute onset of haematochezia. Symptoms began 2 days earlier when she developed nausea and vomiting followed by a 24 h period of multiple episodes of diarrhoea initially with streaks of blood that later progressed to frank haematochezia. She also reported moderate, colicky, cramping-like left lower quadrant (LLQ) abdominal pain. She denied fever or chills. Other medical history included primary hyperparathyroidism status post parathyroidectomy, glaucoma and post-traumatic stress disorder. Prescribed medications included brimonidine and travoprost eye drops, enalapril, verapamil and paroxetine.

Family history was significant for heart disease in her mother but no other known medical problems including malignancy and inflammatory bowel disease. The patient had a distant 5-pack-year smoking history but denied any alcohol or illicit drug use.

On admission, she was afebrile with an elevated blood pressure of 166/89 mm Hg, but she had not taken her antihypertensive medications since the start of her symptoms. Physical examination was significant only for mild LLQ abdominal pain with no rebound tenderness, rigidity or other peritoneal signs. Bowel sounds were present but hypoactive. While in the ED, she had a bowel movement containing bright red blood.

INVESTIGATIONS

Admission laboratory tests were significant for lactic acidosis at 3 mmol/L and leukocytosis at $22.3 \times 10^9/L$ (85% neutrophils with no bands). A basic metabolic panel, hepatic function panel, amylase and lipase were all within normal limits. Her initial haemoglobin and haematocrit were 14.8 g/dL and 42.1%, respectively. Platelets were normal at $312 \times 10^9/L$. Blood cultures showed no growth. Stool samples showed 4+ faecal leucocytes but were negative for enteric pathogens and *Clostridium difficile*.

A contrasted CT of the abdomen/pelvis revealed long-segment, abnormal wall thickening involving the splenic flexure and descending colon with only trace inflammatory changes in the left pericolic gutter suggestive of colitis. No atherosclerotic

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changes were noted in any of the splanchnic vasculature. Colonoscopy revealed oedematous, friable mucosa with overlying exudate extending from the proximal sigmoid/descending colon (at approximately 40 cm) up to the splenic flexure. There was clear demarcation of normal mucosa in the distal sigmoid and in the distal transverse colon on either side of the affected area, consistent with ischaemic colitis. Biopsies showed microscopic evidence of acute inflammation, necrosis and ulceration consistent with ischaemic colitis. The pattern of ischaemia seen on colonoscopy prompted the gastroenterologist to further question the patient about vasoconstrictor medication usage and she recalled taking 'a lot' of a nasal decongestant containing aspirin 325 mg and phenylephrine bitartrate 7.8 mg for a recent episode of sinusitis and nasal congestion.

OUTCOME AND FOLLOW-UP

The patient made an uneventful recovery. She was afebrile throughout the hospital course with improvement in abdominal pain and resolution of haematochezia, nausea, vomiting and laboratory abnormalities with supportive therapy. At the time of discharge, haemoglobin and haematocrit stabilised were 10.6 g/dL and 30.9%, respectively.

DISCUSSION

There were eight reported cases of ischaemic colitis associated with pseudoephedrine use but none were due to phenylephrine use.^{1–5} Six were women ranging between 37 and 58 years and two men aged 33 and 46 years. All of these patients presented with similar episodes of abdominal pain and haematochezia. One case resulted in a hemicolectomy due to long-term pseudoephedrine use that was followed by an ileocolic resection 4 months later secondary to reuse of the medication.³ Once the α -agonist drug was removed, there were no further reports of colitis among any of the patients.

In six of the case reports the patients' initial presentation showed a mild-to-moderate leukocytosis ($12.0\text{--}18.7 \times 10^9/\text{L}$). The other two cases did not report laboratory findings.^{3,4} All the patients had little-to-no gastrointestinal history, but had a significant pseudoephedrine use history that was either heavy, chronic, daily or recent at an Food and Drug Administration recommended dose. In all of the cases except for the one resulting in an ileocolic resection,³ a colonoscopy was performed that showed evidence of segmental colitis. All but one patient⁵ had biopsies confirming ischaemic colitis as well.

The most frequent causes of ischaemic colitis are arterial embolism and thrombosis, accounting for 65–75% of cases.¹⁰ Our patient showed no atherosclerotic changes on CT scan in the area of colonic inflammation and thus represents one of the 20% with non-occlusive aetiology. Non-occlusive ischaemic colitis can be due to hypovolaemia, hypotension, reduced cardiac output and α -adrenergic agonists. Our literature search, however, found no reports of phenylephrine-associated ischaemic colitis, but only reports of pseudoephedrine-associated ischaemic colitis. In comparison, our patient's history and physical examination, colonoscopy, laboratory findings and biopsy are all consistent with the findings in the previously published case reports aforementioned. Where our patient's case differs, then, is in the active ingredient in her choice of cold medication.

We discovered that several pharmaceutical companies who had previously used pseudoephedrine as the active ingredient in

their cold medications have switched to using phenylephrine. Indeed, the company that manufactured our patient's choice of over-the-counter medication switched all of their pseudoephedrine containing products to phenylephrine containing products in 2006.¹¹ Our patient's presentation of acute ischaemic colitis after the use of phenylephrine suggests that there continues to be a potential adverse effect using over-the-counter cold medications, even with this less potent nasal decongestant. Although we are presenting the first case report of ischaemic colitis associated with phenylephrine, we suspect other presentations will follow now that phenylephrine is the more common active ingredient in cold medications.

Learning points

- ▶ Phenylephrine is the more common active ingredient in over-the-counter (OTC) cold medications. Healthcare professionals must be aware of the dangers of common OTC medications and should counsel patients to use them with caution.
- ▶ All healthcare professionals should be reminded of the importance of questioning patients on their use of prescribed and OTC medications.

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