Clinical Study

Phenolphthalein abuse presenting as reversible renal failure

Sourabh Sharma[1], A. K. Gadpayle[1], Harish Kumar Gupta[1], Naveen Kumar[1], Neha Sharma[2]

[1]*Dr Ram Manohar Lohia Hospital, New Delhi, India*

[2]*Dr S.N. medical college, Jodhpur, Rajasthan, India*

Received: 15 April 2017 Revised: 23 April 2017 Accepted: 3 May 2017

Abstract

Objective: Phenolphthalein is habit forming laxative and is available as over-the-counter drug in developing countries. Chronic consumption of Phenolphthalein can damage any organ system. Its use should be strongly discouraged. **Materials and methods:** A 38 years old female presented with abdominal pain, decreased urine output, nausea and weakness for two weeks. In past she had abdominal Koch's in 2005 and following that multiple admissions in surgical unit for sub-acute intestinal obstruction. **Results:** On evaluation she had deranged renal function, severe hypocalcemia, hypokalemia, hypomagnesemia, metabolic acidosis with increased anion gap, and severe anaemia. On third day of admission, repeated enquires for possible cause of these derangements revealed that she was abusing over-the-counter available Phenolphthalein as laxative for last 6 years. Within one week of stopping phenolphthalein, her deranged kidney functions and electrolyte disturbances improved. **Conclusion:** Phenolphthalein was used as laxative in past, but was banned in 1990s because of potential carcinogenic role. However, in developing country like India, it is still available freely. The case emphasise the fact that patients can present with complications of over-the-counter banned drugs and detected in time, Phenolphthalein toxicity is reversible with supportive care.

Keywords: Phenolphthalein, Acute kidney injury, laxative abuse, metabolic acidosis

Introduction

Phenolphthalein has been used as a laxative for decades. In 1990s, when it was found that it is a potential carcinogen, it was banned in U.S. and many European countries. Even after two decades of ban, it is still available in countries like India. We present this case to emphasise the fact that phenolphthalein abuse can present even in today's world and one should be aware about it. Though fatal phenolphthalein poisoning is rarely reported in present century, still it is happening because of its over the counter availability.

Case presentation

A 38years old female presented to emergency department with complaints of abdominal pain, decreased urine output, nausea and weakness since last two weeks. She also had complaint of diffuse bony pain and intermittent swelling over face and limbs. There was no history of fever, diarrhoea, hematemesis, change in colour of urine or any history of altered sensorium. She was a diagnosed case of nutritional anaemia and was on haematinics. There was a past history of abdominal tuberculosis in 2005 for which she took complete treatment for 6 month. Following that she was admitted on multiple occasions in surgical unit for sub-acute intestinal obstruction and use to suffer from sever constipation. On examination, her blood pressure was 90/60mmHg, pulse rate 114/minute, temperature 97.1°F and respiratory rate of 18/minutes. She was dehydrated and pale, but there was no icterus, cyanosis, lymphadenopathy or clubbing. On abdominal examination, there was no organomegaly, free fluid in peritoneal cavity or renal angle tenderness. Rest of systemic examination was normal.

On subsequent enquires, she gave history of laxative abuse. She used to take phenolphthalein tablets (190mg

**Address for Corresponding Author:*

Dr. Sourabh Sharma

Department of Medicine, PGIMER and Dr Ram Manohar Lohia Hospital, New Delhi-110001

Mobile No: +91-9599702038;

Email: drsourabh05@gmail.com

each) available over-the-counter since last 6 years. Sometime she has to take very large numbers of pills, as high as 20 to 40 a day. In summer, her constipation used to increase and she had to increase her dose of laxative. In last few weeks, she was on high dose of phenolphthalein; up to 40 tablets a day.

Investigations

She was having severe normocytic normochromic anaemia (haemoglobin- 3.8gm%) with mean corpuscular volume of (MCV) 88fl (78-94fl), and iron profile suggestive of anaemia of chronic disease. Kidney functions tests were deranged with serum urea 114mg%, serum creatinine 5.2mg% and uric acid 9.6mg%. There was severe hypocalcemia (7.5mg/dl; 8.5-10.5mg/dl), hypokalemia (2.5mEq/l; 3.5-5mEq/l), hypomagnesemia (non-traceable), metabolic acidosis (pH7.28) with base deficit of 9mEq/l and increased anion gap. ECG findings (figure 1) supported the presence of severe hypocalcemia and hypokalemia. Her serum chloride and sodium levels were normal. ELISA for viral markers and HIV were non reactive. She was ANA negative and CRP levels were within normal range. On ultrasonography, kidneys were bilaterally normal.

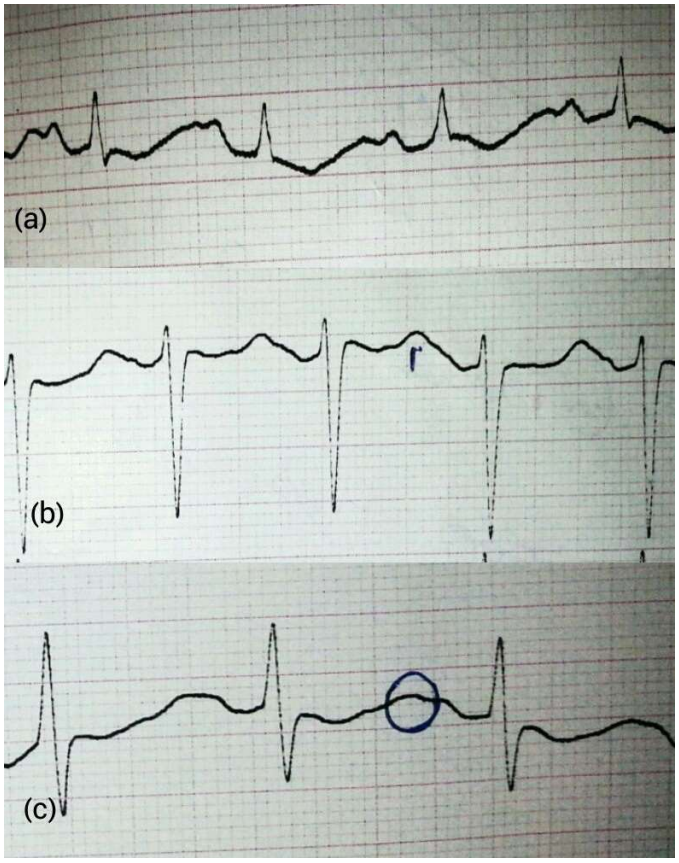

Figure 1. ECG depicting (a) ST depression and U waves suggesting hypokalemia; (b), (c) strips showing QT prolongation suggesting hypocalcemia

Treatment

Patient was given intravenous sodium bicarbonate, calcium gluconate, magnesium sulfate and potassium chloride. She was transfused three units of packed cells during her stay. She was treated on the lines of chronic kidney disease till she was found to be case of laxative abuse.

Discussion

Phenolphthalein is a diphenylmethane cathartic. It is available in white (pure) or faintly yellow (impure) preparation. Only up to 15% of the therapeutic dose of phenolphthalein is absorbed and rest is excreted in the faeces (Lambrianides, 1984). It is mainly eliminated by kidney from the body (Lambrianides, 1984). A portion of the drug absorbed from the intestine are excreted in bile. This enterohepatic circulation contributes to prolongation of its cathartic effect (Lambrianides, 1984).

The cathartic effect of phenolphthalein was discovered in 1902 by Vamossy and since that time, it was widely employed as laxative (Lambrianides, 1984). In past, United States FDA recommended its clinical use in dose of 50 to 200 mg by oral route. However, the drug went into disrepute because of its carcinogenic effects, as described by US National Toxicology Programme in early 1990s. Following that its use as laxative was banned in US and many other countries. The most important complication of chronic phenolphthalein abuse is loss of normal bowel function leading to laxative dependence and ultimately "cathartic colon". Later is dilated colon with loss of its tone and normal peristalsis, more commonly on right side. Chronic bowel retention lead to changes resembling chronic ulcerative colitis both radiologically and pathologically. Apart from it, various studies has reported many other complications: dermatological [epidermal necrolysis (Potter , 1960), erythema multiforme (Baer, 1967), fixed drug eruptions], gastro-intestinal [acute pancreatitis (Lambrianides, 1984), gastrointestinal bleeding, protein-losing gastroenteropathy], haematological [iron-deficient anaemia, disseminated intravascular coagulation], hepatic [fulminant hepatic failure], neurological [encephalitis (Kendal, 1954)] and multiple organ damage in cases of massive overdose (IARC, 1972). Its overdose commonly present with GI disturbances [abdominal pain, diarrhoea, vomiting with intestinal colic (Knox, 1958), malabsorption, steatorrhea], renal and electrolyte imbalance [polydipsia, polyuria, dehydration, hypokalemia, hypocalcemia, metabolic acidosis or alkalosis, deranged kidney functions], cardiac arrhythmia and muscle weakness (IARC, 1972). Many of the systemic disturbances like of kidney, muscle and central nervous system are secondary to electrolyte imbalance (IARC, 1972). Renal failure in association with laxative

abuse has been reported in past (Copeland, 1994). Laxative leads to loss of intestinal sodium and water thus stimulating compensatory rennin-aldosterone axis. Secondary hyperaldosteronism lead to sodium conservation and hypokalemia. Later is associated with rhabdomyolysis which can contribute to renal insufficiency. Moreover, direct renal injury could also be contributing to renal failure. The management of toxicity is conservative as no antidote is available.

Our patient was habitual abuser of phenolphthalein. She used to take more amount of drug in summer season as dehydration aggravated constipation. We conclude that long term abuse of phenolphthalein caused electrolyte imbalance and dehydration which induced kidney failure and probably acute tubular necrosis. Gradually, her symptoms resolved and blood parameters came within normal range once her medication was stopped.

Conclusion

Phenolphthalein is habit forming laxative and is available as over-the-counter drug in developing countries. Chronic consumption of Phenolphthalein can damage any organ system. Its use should be strongly discouraged. In our case, within one week of stopping phenolphthalein her symptoms improved and on 10^{th} day of treatment her serum urea and creatinine was 38 and 1.1mg% respectively. Management of toxicity is conservative. In countries where phenolphthalein is still available, governments should be sensitized towards its potential carcinogenic tendency and it should be banned.

References

Baer RL, Harris H. 1967. Types of cutaneous reactions to drugs. Importance in recognition of adverse reactions. Journal of American Medical Association, 202(3): 710-3.

Copeland PM. 1994. Renal failure associated with laxative abuse. Psychotherapy and Psychosomatics, 62(3-4):200-2.

IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972. Accessed on 18 January 2017. http://monographs.iarc.fr/ENG/Monographs/vol76/mono76-15.pdf

Kendal AC. 1954. Fatal case of encephalitis after phenolphthalein ingestion. British Medical Journal, 2:1461-2.

Knox EG. 1958. A new pink disease. Lancet, 271: 588-9.

Lambrianides AL, Rosin RD. 1984. Acute pancreatitis complicating excessive intake of phenolphthalein. Postgraduate Medical Journal, 60(705):491-92.

Potter B, Auerbach R, Lorincz AL. 1960. Toxic epidermal necrolysis. Acute Pemphigus. Archives of Dermatology, 82:903-7.