Case Report

HYPONATRAEMIA DUE TO ENALAPRIL

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ABSTRACT

A middle aged man presented with muscle cramps. He was found to be having hyponatraemia and mild rhabdomyolysis, due to Enalapril, which he had been using for hypertension. The symptoms improved and biochemical abnormality disappeared after stopping the drug.

KEY WORDS: Hyponatraemia, Enalapril, Rhabdomyolysis.

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INTRODUCTION

Iatrogenic or hospital acquired hyponatraemia is a frequently encountered problem in geriatric population.[1] Most of these cases are mild but can quickly progress to more dangerous levels during therapeutic management of other disorders if overlooked. Severe hyponatraemia (serum Na <120mmol/l) is associated with substantial morbidity and mortality.[2,3] ACE inhibitors are a group of the drugs which are frequently used for the treatment of hypertension and congestive cardiac failure. They have a potential to cause mild to severe hyponatraemia, alone or in combination with other drugs.[6-9] It is always important to identify even milder degrees of hyponatraemia in hospitalized patients because mortality rates are higher in patients with even asymptomatic degrees of hyponatraemia compared with normonatraemic patients.

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CASE REPORT

A 55 year old man, working as an administrator in an office, presented with a couple of days history of frequent muscle cramps in lower limbs and chest cage, generalized weakness and restlessness. He had not been feeling comfortable generally for about two months, having muscle cramps off and on, but never so frequent or severe, as at that time. He was a known hypertensive and was using enalapril 5mg daily for many months. He was on strict salt restricted diet due to a couple of raised blood pressure readings in the previous week. On examination, he was a middle aged man of average built, looking restless. His pulse rate was about 70bpm, blood pressure 130/90mm Hg and respiratory rate 16 per minute. Hydration was fair. Chest and heart were normal on auscultation and rest of the systemic examination including neurological examination was unremarkable. ECG was normal. Serum creatine phosphokinase (CPK) was 1139u/l, SGOT 27u/l and LDH 185u/l. CK-MB was not significantly raised and troponin-T test was negative. Serum sodium was 126mmol/l, potassium 3.8mmol/l, chloride 96mmol/l, urea 3.9mmol/l and creatinine 70umol/l. Haemoglobin was 14.2g/dl and WBC count $9.7x10^9$ /l. Random blood sugar was 6.7mmol/l and fasting total cholesterol was 184mg/dl. A diagnosis of hyponatraemia due to enalapril in the presence of strict salt

restriction was made, which had led to muscle cramps, rhabdomyolysis and raised creatine phosphokinase. Enalapril was stopped and patient was advised to use salt normally. Fluid was not restricted as hyponatraemia was not severe. ECG remained normal on serial monitoring. Serum CPK gradually came down, while SGOT and LDH remained within normal limits. Serum sodium gradually rose to 132mmol/l in next four days. Basal serum cortisol level and TSH and T_4 were well within normal limits. Hypertension got adequately controlled with amlodipine 5mg daily. About two weeks later, patient was absolutely calm and comfortable. Serum sodium was 136mmol/l, potassium 4.4mmol/l and CPK 60u/l.

DISCUSSION

Drug induced hyponatraemia is commonly associated with diuretics, selective serotonin reuptake inhibitors and antiepileptics.[4,5] With increasing polypharmacy and an aging population, the prevalence of drug induced hyponatraemia is likely to increase. Angiotensin converting enzyme inhibitors are a group of vasodilators which are frequently used for the treatment of hypertension and congestive cardiac failure. They have been found to cause significant hyponatraemia occasionally, alone[6-9] or in combination with diuretics[10] or salt restriction.[11] Approximately 20 cases of severe hyponatraemia with ACE inhibitors have been reported in literature.[12]

ACE inhibitors in antihypertensive doses may block conversion of angiotensin I to angiotensin II in the peripheral circulation but not in the brain. Increased circulating angiotensin I enters the brain and is converted to angiotensin II, which may stimulate thirst and release of ADH from the hypothalamus, eventually leading to hyponatraemia.[12-14]

Assessment and management of a patient with hyponatraemia depends on the clinical status and the likelihood that one or more drugs are responsible. Most hyponatraemic patients would be asymptomatic. Patients with moderate to severe hyponatraemia may present with symptoms like anorexia, nausea, restlessness, muscle weakness, spasm or cramps, confusion, irritability, convulsions and coma. Alternative explanations for these clinical features should always be considered. Conditions which may be responsible for hyponatraemia like cardiac, liver and renal failure should be ruled out. A careful history, examination and clinical assessment of fluid status are needed to exclude non drug causes of hyponatraemia. Raised blood sugar or urea level, pseudohyponatraemia due to hypertriglyceridaemia and paraproteinaemia and other occult co-morbidities like hypothyroidism and hypoadrenalism should be excluded. Syndrome of Inappropriate Anti Diuretic Harmone due to some malignancy or CNS lesion should also be looked for.[13]

In mild to moderate cases of ACE inhibitors induced hyponatraemia or drug induced hyponatraemia with a normovolaemic fluid status clinically, ceasing the offending drug and gentle fluid restriction would improve serum sodium levels gradually within a week. In an acutely unwell patient due to severe drug induced hyponatraemia, severe fluid restriction or infusion of hypertonic saline may be required.[12-14] ACE inhibitors have some potassium retaining properties but serum potassium level usually remains within normal limits when an ACE inhibitor is used alone. Patients may show hypokalaemia if thiazide or loop diuretics are used concomitantly with ACE inhibitors.[4]

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Book Review

PATHOPHYSIOLOGIC BASIS OF ACID-BASE DISORDERS

By Farrokh Habibzadeh, MD, Mahboobeh Yadollahie, MD
Published by Navid Publication; PO Box: 71365-666, Shiraz, Iran. Pages: 216 ISBN: 964-358-436-4.

The monograph on PATHOPHYSIOLOGIC BASIS OF ACID-BASE DISORDERS by Farrokh Habibzadeh and Mahboobeh Yadollahie from Siraz, Islamic Republic of Iran is a laudable accomplishment.

The first four chapters deal with the elementary concepts of acid-base related physical chemistry and respiratory physiology. These concepts are essential for understanding the basic mechanisms underlying acid-base disorders. Things to remember at the end of each chapter offer a good opportunity to test how good concepts have touched the cognition. However, an abridgement of the first four chapters might ease the switch over to the following chapters including cases of acid-base disorder. For the sake of brevity and integration, authors should consider to include chapter 8 after third one.

The chapter on the introduction to acid-base chemistry and ABGs is well organized as a template to understand the pathophysiology underlying the disorders. However, an allocation of a page or two on the principles of electrometric or optical measurement of blood gas parameters of the analyzer might be of added advantage. This may help in the interpretation of ABGs in context of source of errors and accuracy study of the blood gas analyzer.

The chapters 5 and 7 on the clinical cases of acid-base disorders are lucidly written. Associated changes in anion gap and electrolytes are well integrated to ease understanding the underlying mechanisms of disorders. Thus, this book may prove to be a good guide in PBL or CPBL curriculum especially during clerkship and residency when it comes to application of concepts in understanding a problem to derive a solution.

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