WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 13, Issue 2, 257-265. Review Article ISSN 2277–7105

CARBAMAZEPINE INDUCED HYPONATREMIA (ACUTE ENCEPHALOPATHY SHOCK)

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Article Received on
22 Nov. 2023,

Revised on 12 Dec. 2023,
Accepted on 02 Jan. 2024

DOI: 10.20959/wjpr20242-30956

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ABSTRACT

Carbamazepine-induced hyponatremia is a rare condition. The patients may or may not be symptomatic. Epilepsy is considered a social taboo. Hence, patients do not reveal history of being on antiepileptic agents. Carbamazepine is a known antiepileptic and psychotropic agent. It is commonly used for the treatment of seizures and psychiatric disorders. We present a case of 70 year old female patient was admitted in the MICU department with the history carbamazepine induced hyponatremia. It raises antidiuretic hormone (ADH) levels. This leads to increased sensitivity of renal tubules to ADH levels. Final diagnosis was carbamazepine induced hyponatremia with Acute Encephalopathy, shock on examination Echo (outside)-LVH, Normal LV function, Mild AR, MR, No PE/Clot, (outside)-sinus rhythm, Qt interval increased, ECG-Sinus tachycardia. She recovers significantly Hence, it is essential to monitor sodium levels in patients on carbamazepine therapy and also on drugs with similar mechanism of action.

KEYWORDS: Anti diuretic hormone, Antiepiletic agent, Seizures, Endothelial dysfunction.

INTRODUCTION

Hyponatremia

- Hyponatremia is defined as a serum sodium (Na+) level of < 136 mmol/L, and is considered significant when levels are between 115 and 125 mmol/L. Acute hyponatremia (less than 48 hours) can cause neurologic complications such as seizures and coma and it necessitates urgency of care to prevent complications.[1-6]

Serum [Na+], mEq\L[3]

- Severe Hyponatremia lesser then 125
- Moderate hyponatremia 125-130
- Mild hyponatremia 130-135

Carbamazepine often causes drug-induced hyponatremia. Hyponatremia presents a variety of symptoms and sometimes affects life.

The incidence of hyponatremia due to CBZ has been reported to be 1.8%-40%.

CBZ stimulates antidiuretic hormone (ADH) secretion and that the excess ADH binds to ADH receptors of the renal collecting tubules, resulting in cyclic adenosine monophosphate (AMP) production and excessive enhancement of the water permeability of the collecting tubules.

Treatment usually involves removal of the drug in most cases.[7-8]

Encephalopathy: Hyponatremic encephalopathy is defined as central nervous system dysfunction due to hyponatremia and occurs when brain fails in regulating its volume. The most striking and severe symptoms of HNE are related to the compression of the brain parenchyma against the rigid skull. In severe cases, brain herniation and death often occurs preceded by seizures and coma. The symptoms often occur during acute and profound hyponatremia because the brain has no or little time to adjust to hypo-osmolality. Severe symptoms can also occur after acute on chronic hyponatremia, or even after moderate acute hyponatremia.

Most patients with hypovolemic hyponatremia can be treated successfully with isotonic saline solution (0.9% NaCl), but in the presence of severe symptoms, such as seizures or coma, hypertonic saline infusion is required.[9-11]

Shock: Sepsis is a life-threatening organ dysfunction caused by an irregular host response to infection. There are cytokines that regulate various inflammatory responses. Dysregulation of cytokines causes endothelial dysfunction, vasodilation and increased capillary permeability, then causes cellular leakage syndrome that interferes with regulation and intravascular hypovolemia, cellular dysfunction, and ultimately tissue death. Electrolyte imbalances may provide crucial clues to diagnose a sepsis infection, specifically hyponatremia. Hyponatremia is a frequent electrolyte abnormality seen. The C-reactive protein is a second biomarker.[10-12]

Symptoms of sepsis include

A fever above 101ºF (38ºC) or a temperature below 96.8ºF (36ºC)

Heart rate higher than 90 beats per minute

Breathing rate higher than 20 breaths per minute

Probable or confirmed infection

There must be two of these symptoms to diagnose sepsis.

Treatment day 1

Intravenous antibiotics to fight infection

Vasopressor medications, which are drugs that constrict blood vessels and help increase blood pressure

Insuline for blood sugar stability

Corticosteroids

Large amounts of intravenous (IV) fluids will be administered to treat dehydrationn and help increase blood pressure and blood flow to the organs. A respirator for breathing may also be necessary.

Chief complaints: unresponsive since 1 day, vomiting (non projectile, not blood stained, contained food and water)

Vitals

BP- right arm-160/80 mmHg -it arm-120/80 palpatory method

PR-98

Pt is sleepy, arousable to call, obeying commands

GRBS-130

System review

CNS: GCS-E3V5M6, Plantars

CVS-S1, S2+

RR-15 MIN

Sp02-95% (on 6 litres O2)

Past medical history

HTN since 10-15 years

Trigeminal Neuralgia since 10 years

Lumbar fixation 1 year back (disc prolapse)

Right eye exonerations secondary to trauma 12 years back

Drug history

Tab Telma AM 80 mg BD (Telmisartan)

Tab Zeptol CR 200 mg BD (Carbamazepine controlled release tablets)

Tab Pentanerv NT 100 MG OD H/S (Gabapentin+Nortriptyline)

Tab Eslizen 400 mg OD (Eslicarbazepine)

Tab Gabapir 300 MG BD (Gabapentin)

h/o drug abuse carbamazepine (BD to TID since 2 days)

dizzy and after which 1 episode of vomiting (a/w decreased apetite and nausea since 1 day)

Increased unresponsiveness (decreased verbal response) Apetite, Taken to other hospital.

BP was 50/40; HR-112; sp02-85%; GRBS-153mg/dl Started. Noradrenaline(infusion) BP improved.

Came to this hospital due to financial.

OBJECTIVE

Echo (Outside)- LVH, Normal LV function, Mild AR, MR, No PE/Clot

ECG (Outside)-sinus rhythm, Qt interval increased

ECG-Sinus tachycardia

Lab investigations

Serium electrolyte

Electrolyte	Day 1	Day 1	Day 1	Day 2	Day 4	Day 6	Normal values
Sodium	125	130	133	133	136	136	135-145
Potassium	2.88	3.4	3.2	3.2	3.3	4.1	3.5-5.5
Chloride	94	94	95	94	95	99	95-105

ABG

Parameter	Day 1	Day 2	Normal range
pH	7.38	7.39	7.35-7.45
pCO2	46.9	46.9	35-45 mmHg
pO2	39	37	80-100 mmHg
HCO3	25.5	27.6	22-27 ml equivalents

CBP

Parameter	Day 1	Day 2	Day 3	Normal range
Hb	12.0	10.0	10.9	11-15gm/dL
Wbc	14,680	33,430	13,300	4,000-11,000/cumm
Platelet	1.94 lakh	2.09 lakh	2.02 lakh	1.8-4.5 lakhs/cumm

HRCT

Pro-BNP: 721 pg/ml (<125 pg/ml)

D-dimer-849.16 (<500 n/ml)

RFT

Parameter	Day 1	Day 2	Normal range
Blood Urea	15	22	13-43 mg/dL
Ser. Creatinine	0.7	0.6	0.5-1.1 mg/dL

CT Brain

MDCT image morphology suggestive of parenchymal volume loss

CPK-MB- 26.3 U/L (upto 25 U/L)

Final diagnosis was carbamazepine induced hyponatremia (Acute encephalopathy, shock)

Day notes

The day the patient have given **cardiology opinion such as** Cardiology opinion- BP-120/80, PR-125/min, 2D echo-Good LV function, Continue T. Atorvas, T. Clopitab and **neurology opinion such as** Attacks occur once in 2 months**,** This attack occurred after 6 months lasting**,** For 2 minutes, multiple times per day**,** Presently 2-3 episodes

O/E:pt is conscious, irritable, responding to VC

Advice: Tab Gabapentin 400 mg BD

W/H Carbamazepine, MRI-CISS after Patient stabilises.

On the next day PR:123/mt (Rt radial pulse), radial pulse-feeble, BP:Right arm-160/90 mmHg, Left arm-120, RR-18/min, wheezing, SpO2-94%, Plantars, moving all 4 limbs, O/E:Patient is arousable to commands, b/l ankle oedema, Advice:Inj Noradrenaline IV infusion @5ml/hr 6 lit o2/min, Inj Noradrenaline taper and stop, Stop antihypertensives, Inj Magnex Forte, Add T.Claribid 500mg,T.Gabapin 200 mg, Inj Piptaz D-dimer, Trop I, Pro BNP, 2D Echo.

On third day O/E:severe pain in left eye, headache, , wheezing • BP-130/90 • HR-141/min • Plantars decreased • Advice-Stop Inj Piptaz and continue Inj Ampitrust, Add Tab Pentanerv NT stat.

On fourth day Encephalopathy and shock resolved • c/o-facial lt side pain • PR-111/min

Neuro opinion

-Tab Zeptol CR 200 mg

Add Inj Meaxon plus in 100 ml NS over 1.2 hr

Stop Pentanerv NT.

On fifth day Neuro opinion

c/o – pain, Tab Gabapin 400 mg BD, Tab Eslizen 600 mg OD, Tab Pregnable 75 mg OD, Tab Pexcep, -CR-12.5 MG BD, Lignocaine gel for L/A

Advice -surgery for intractable neuralgia

Cardio opinion

O/E:PR -80/min, BP-130/80 mmHg, ECG -NSR, 2D Echo -good LV function, Inj Heparin 5000 U TID, T.Clopitab A

Treatment

Drug	Generic Name	Dose	ROA
Inj Magnex Forte	Cefoperazone+ Sulbactum	2 gm	IV
Inj Pan	Pantoprazole	40 mg	IV
Inj Zofer	Ondansetron	4 mg	IV
Inj Noradrenaline	Noradrenaline	5 ml	IV
Inj Ampitrust	Ampicillin+Sulbactum	1.5 gm	IV
T.Clopitab	Clopidogrel	75 mg	PO
T.Atorvas	Atorvastatin	10 mg	PO
IVF NS	Normal Saline	75 ml	IV
Inj Pentanerv NT	Gabapentine +Nortryptiline	100 mg	PO
T.Claribid	Clarithromycin	500 mg	PO
T.Gabapin	Gabapentin	300 mg	PO
Inj Piptaz	Piperacillin+Tazobactum	4.5 g	IV
Tab Zeptol CR	Carbamazepine	200mg	PO
Inj kcl	Potassium chloride	20meq	Iv
Syp potklor	Potassium chloride	10ml	Po
Neb levolin budecort	Ipratropium bromide, salbutamol	-	N

75/150 OD, T.Atorvas 40 mg OD, T.Met XL 25 mg OD, T.Ivabrad 5 mg BD, T.Ismo 10 mg BD

Advice -CAG.

On sixth day O/E: PR-80/min

- BP-130/80 mmHg
- Patient does not want to stay and get discharged
- Advice: Stop Inj Heparin.

Plan after discharge

CAG and MVD for trigeminal neuralgia after the patient stabilises.

CASE DISCUSSION

Carbamazepine, an anticonvulsant and psychotropic drug, is used commonly for the treatment of epilepsy, neuralgia, mental retardation and psychiatric disorders.[15] The incidence of hyponatremia (Na<134 mEq/L) in 451 carbamazepine-treated patients was 13.5% and that of severe hyponatremia ((Na<128 mEq/L)) was 2.8%. Advanced age was a risk factor for hyponatremia.[16] Hyponatremia, both symptomatic and asymptomatic, has been found to be directly related to increased mortality and morbidity of hyponatremia such as medications like diuretics, antiepileptics, and antipsychotics. Diuretics are the most common cause of hyponatremia. In our case, hyponatremia was caused by carbamazepine. Carbamazepine is commonly used for the treatment of seizures, neuralgia, and psychiatric disorders. Carbamazepine-induced hyponatremia is more common in females, patients of age more than 40 years, low baseline serum sodium levels, psychiatric illness, surgery, and hypothyroidism.[17,18] Our patient had two risk factors – age and gender. Carbamazepine causes increase in antidiuretic hormone (ADH) which leads to abnormal sensitivity of renal tubules to ADH activity. This causes increased expression of aquaporin 2 channels in the renal tubules.[19] The incidence of hyponatremia due to carbamazepine has been found to be 1.8%–40% in previous studies. Although the incidence of hyponatremia with monotherapy of carbamazepine is low, the overall incidence is on the rise. Other anticonvulsants causing hyponatremia are oxcarbamazepine and lamotrigine. All these drugs alter the vasopressin levels in the renal tubules.[20] The incidence of drug-induced hyponatremia is on the rise as a result of polypharmacy and self-medication especially in the elderly patients. A few case reports described in the past have highlighted the role of genetic predisposition in the development of drug-induced diabetes insipidus. However, this association was not observed in cases of drug-induced hyponatremia such as diuretics. Thus, it was concluded that patients developing hyponatremia as a result of diabetes insipidus with one drug can be affected with another drug affecting vasopressin secretion in the renal tubules. Since epilepsy is considered a social stigma and patients are hesitant to share the history of being on antiepileptic drugs, one can miss this rare cause of hyponatremia. The geriatric patients usually go to a family physician as the first contact for medical services. Drug-induced hyponatremia, although a known entity, is rarely documented. As the geriatric patients have underlying comorbidities and age-related physiological changes, even a minimal change in the electrolytes can lead to morbidities and avoidable mortality. This case highlights the importance of consideration of the side effects of these often-prescribed medications in aged population.

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 other 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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