

Hyponatremia Following Losartan Therapy In A Patient Of Cerebro Vascular Attack

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Abstract: Electrolyte imbalances are frequently encountered with the use of Losartan. Losartan is a first line drug used for hypertension with less side effects. Herein we report a case of a 60year old male patient presenting to EMD(Emergency medicine Department) with slurred speech & vomiting 3-4 times for past 1week who developed hyponatremia secondary to losartan. Patient is a known case of cerebro vascular attack since 3years, had associated hypertension and diabetes for last 10years. On admission patient's serum sodium level was 119meq/l which improved by daily sodium infusion. Hyponatremia can emerge as a serious adverse effect of losartan therapy, although not much documented in scientific literature. [Shah V Natl J Integr Res Med, 2019; 10(4):83-85]

Key Words: Hyponatremia, Cerebrovascular attack, Losartan, Hypertension

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Introduction: Electrolyte imbalance is a very common entity occur in the patients of multi drug therapy and multiple co-morbidity. Losartan is a Angiotensin1 (AT1) receptor antagonist potently and selectively inhibits most of the biological effects of angiotensin II like pressure responses, vasopressin release, release of aldosterone and adrenal catechol amines, enhancement of noradrenergic neurotransmission, increases in sympathetic tone, changes in renal function, etc. It is an approved and preferred first-line drug in hypertension with a favorable safety profile.¹

Losartan is a angiotensin receptor blocker(ARB). Hyponatremia with losartan is a chance occurrence; it may be explained by the hypothesis that AT₁ receptor inhibition causes an angiotensin II-mediated decrease in renal tubular sodium reabsorption and reduced aldosterone release, resulting in hyponatremia. It may also causes hyperkalemia as ARBs reducing blood pressure along with it induction of a rise in serum potassium levels leading to hyperkalemia.²

Case Report: Herein we report a case of hyponatremia, who is a 60 year old diabetic and hypertensive male patient presenting to EMD with slurred speech and vomiting 3-4 times for past 1week. Patient is a known case of cerebro vascular attack since 3years, had associated with hypertension and diabetes for last 10years. He was treated with Losartan 50mg once daily and Nifedipine10mg twice daily for hypertension and combination of Metformin + Glimepiride to control diabetes since last 10years. Patient was bedridden since last 3years. He was also on Trimetazidine and Nifedipine since last 3years. He

was socially neglected in terms of oral feeding and nursing . Routine blood tests were normal. He had no other relevant medical or surgical history. He was taking no other concomitant medications except these. On admission the patient's GCS(Glasgow Coma Scale) Score was E4V1M3. The pulse rate was 78/min and blood pressure was128/86 mmHg. He had dehydration on admission. During his duration of admission he had an attack of convulsion.

CT brain was done which revealed gliotic area in right temporal and occipital periventricular white matter corresponding to old insults in brain. Patient was continued with Losartan along with Levetiracetam, Clopidogrel, Insulin and other supportive therapy.

Hyponatremia was managed with infusion of 0.9% sodium in normal saline upto 2L per day for 4days. His sodium level was gradually corrected and sensorium also improved. His input output balance on 2nd & 3rd day alternatively was 1370ml & 1735ml. Dehydration was corrected by this positive balance.

He was discharged after 5days in a stable condition with normalization of blood reports. He was prescribed Nifedipine 10mg twice daily and Losartan 50mg once daily for controlling blood pressure & for diabetes same Metformin +Glimepiride combination. Dietary advice of two table spoon(~10gm) extra salt on daily basis. This case was reported via Vigiflow at WHO-UMC ADR no 2019-39972 as a Losartan induced hyponatremia.

Table1: Serum Sodium levels from admission to discharge.

Day of admission	119meq/l
2 nd day	122meq/l
3 rd day	124meq/l
4 th day	130meq/l
5 th day	134meq/l

Discussion : Hyponatremia is diagnosed when sodium levels fall below 135meq/L. Hyponatremia in patients with an acute central nervous system disease is the most common electrolyte disturbance encountered in neurological intensive care units.³ Our patient had an acute attack of convulsion & also found gliotic area in it's right temporal region. Hyponatremia can present with signs and symptoms mimicking a neurological disease and can worsen the existing neurological deficits.³ Hyponatremia is one of the important causes of persistent altered sensorium in stroke patients. It can also give various other neurological sign and symptoms like seizures, which can further deteriorate level of consciousness and outcome.⁴ Hyponatremia represents a frequent cause of epileptic seizures, as shown in a recent prospective observational multicenter study where acute epileptic seizures and focal neurological deficits were identified in 5% of patients with severe (<125 meq/L) hyponatremia.⁵

Angiotensin II which attaches to AT1 receptors affects vasoconstriction and intravascular volume expansion.⁶ AT1 receptor inhibition causes an angiotensin II-mediated decrease in renal tubular sodium reabsorption and reduced aldosterone release, resulting in hyperkalemia and hyponatremia.⁷

Patient was hypertensive along with diabetic. For that he was taking glimepiride & Metformin. Here losartan & glimepiride can cause drug- drug interaction. Metabolism of losartan by recombinant CYP2C9* 1, CYP2C9*3, CYP2C9*13, and CYP2C9* 16 was inhibited by glimepiride competitively. The inhibitory effect of glimepiride on losartan metabolism by CYP2C9*13 was marginal. On the other hand, losartan weakly inhibited the hydroxylation of glimepiride by P450 2C9 enzymes competitively. These results may provide valuable information for optimizing the anti-hypertension efficacy of

losartan when glimepiride is co-administered to patients.⁸

Patient was also taking Nifedipine along with Losartan. There is a review that patient who continue taking Nifedipine for a long time have significant increase in sodium excretion with a cumulative loss of sodium.⁹

Herein we attribute hyponatremia in above mentioned case to many factors, the patient had a history of cardio vascular attack and was concomitantly on Losartan ,Nifedipine, Glimepride and Metformin. Electrolyte imbalance is more common if drugs are administered to gather as they might have tendency to retard the metabolism of other drugs as mentioned above. Hence careful prescribing should be followed.

Conclusion: Hyponatremia with losartan is a very rare occurrence. It can present with signs and symptoms mimicking a neurological disease and can worsen the existing neurological deficits in a patient .Physicians should have high index of suspicion and rule out hyponatremia in patients taking Losartan, especially in patients who present with the symptoms of altered sensorium, lethargy and dizziness

References

1. Dandan RH. Renin and angiotensin. In: Brunton LL, Chabner BA, Knollmann BC, editors. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 13th ed. New York: McGraw-Hill; 2011.p. 721-44
2. Desai A (2008) Hyperkalemia associated with inhibitors of the renin-angiotensin-aldosterone system: balancing risk and benefit. *Circulation* 118:1609-1611
3. Lath R. Hyponatremia in neurological disease in ICU. *Indian J Crit Care Med.* 2005;9:47-51.
4. Bussmann C, Bast T, Rating D. Hyponatraemia in children with acute CNS disease: SIADH or cerebral salt wasting? *Childs Nerv Syst.* 2001;17:58-62.
5. Nigro N, Winzeler B, Suter-Widmer I, Schuetz P, Arici B, Bally M, Blum C, Bingisser R, Bock A, Huber A, Müller B, Nickel CH, Christ-Crain M *J Am Geriatr Soc.* 2015 Mar; 63(3):470-5.
6. Burnier M. Angiotensin II type 1 receptor blockers. *Circulation.* 2001;103:904-912.
7. Das S, Bandyopadhyay S, Ramasamy A Prabhu VV, Pachiappan S. A case of losartan-

induced severe Hyponatremia J Pharmacol Pharmacother 2015;6:219-21.

8. Sai-Zhen Chen, Pei-Pei Pan, Lei-Bin Shen, Shan-Shan Xu, Da-Peng Dai, Pei-Wu Geng, Jie Cai, Jian-Ping Cai, and Guo-Xin Hu. Drug-drug interaction of losartan and glimepiride metabolism by recombinant microsome CYP2C9*1, 2C9*3, 2C9*13, and 2C9*16 in vitro. 2014; 52: 732-738. doi: 10.5414/CP202071.
9. Francesco P. Cappuccio, M.D., Nirmala D. Markandu, R.S.N., Giuseppe A. Sagnella, Ph.D., Donald R.J. Singer, M.R.C.P., Michelle A. Miller, B.Sc., Martin G. Buckley, B.Sc., Graham A. MacGregor, F.R.C.P.  Correspondence information about the author F.R.C.P. Graham A. MacGregor Blood Pressure Unit, Department of Medicine, St. George's Hospital Medical School, London, United Kingdom

Conflict of interest: None
Funding: None
Cite this Article as: Harkhani J, Gupta S, Sood S, Malhotra S, Patel P. Hyponatremia following Losartan therapy in a patient of Cerebro Vascular Attack. Natl J Integr Res Med 2019; 10 (4):83-85